

L139 5 S L138,L130,L133,L138  
E C23H23NO6/MF  
L140 15 S E3 AND NC5/ES AND C6/ES AND 3/NR  
L141 11 S L140 AND METHOXY  
L142 232 S NC5/ES AND 46.150.18/RID AND 3/NR AND 6/O AND 1/N AND 23/C  
L143 131 S L142 AND METHOXY  
L144 42 S L143 AND DIMETHOXY  
L145 0 S L144 AND DIPHENYL  
L146 0 S L144 AND PROPIONIC  
L147 14 S L144 AND PYRID?  
L148 4 S L147 NOT ESTER  
L149 53 S L143 AND PYRID? NOT L147  
L150 14 S L149 NOT ESTER  
E C22H33NO6/MF  
E C32H33NO6/MF  
L151 4 S E3 AND NC5/ES AND 4/NR  
L152 76 S NC5/ES AND 46.150.18/RID AND 4/NR AND 1/N AND 6/O AND 32/C  
L153 40 S L152 AND PYRID?  
L154 22 S L153 AND ?METHOXY?/CNS  
L155 6 S L154 NOT ESTER  
E C23H22NO4/MF  
L156 2 S E3 AND NC5/ES AND 3 /NR  
L157 1079 S NC5/ES AND 46.150.18/RID AND 3/NR AND 23/C AND 1/N AND 4/O  
L158 431 S L157 AND PYRID?  
L159 105 S L158 AND DIMETHYL  
L160 10 S L159 AND METHOXY  
L161 4 S L160 NOT ESTER  
L162 1504 S NC5/ES AND 3/NR AND 46.150.18/RID AND 1/N AND 3/O AND 23/C  
L163 218 S L162 AND DIMETHYL  
L164 128 S L163 NOT ESTER  
L165 35 S L164 AND PYRID?  
L166 23 S L165 NOT S/ELS

FILE 'HCAPLUS' ENTERED AT 16:02:35 ON 10 FEB 2005

L167 54 S L139  
L168 4332 S L167,L127  
SAV TEMP L168 HADDAD089B/A

FILE 'REGISTRY' ENTERED AT 16:03:33 ON 10 FEB 2005

L169 85 S L114,L124,L139  
SAV L169 HADDAD089C/A

=> => d his

(FILE 'HCAPLUS' ENTERED AT 08:30:51 ON 14 FEB 2005)

DEL HIS

FILE 'HCAPLUS' ENTERED AT 08:32:30 ON 14 FEB 2005

L1 1 S SD186 OR SD 186  
L2 0 S L7418415 OR L() (7418415 OR 741 8415 OR 7418 415 OR 7 418 415)  
L3 0 S SD183 OR SD 183  
L4 1 S SD983 OR SD 983  
L5 5 S XT199 OR XT 199  
L6 2 S SG545 OR SG 545  
L7 5 S SM256 OR SM 256  
L8 0 S SD836 OR SD 836  
L9 3 S SD7784 OR SD 7784  
L10 0 S SD7783 OR SD 7783  
L11 36 S S137 OR S 137  
L12 2 S S787 OR S 787  
L13 3 S S448 OR S 448  
L14 2 S SC68448 OR SC() (68448 OR 68 448)  
L15 3 S SC56631 OR SC() (56631 OR 56 631)

L16 2 S SC69000 OR SC() (69000 OR 69 000)  
 L17 4 S SC65811 OR SC() (65811 OR 65 811)  
 L18 5 S SB223245 OR SB() (223245 OR 223 245)  
 L19 9 S SB265123 OR SB() (265123 OR 265 123)  
 L20 0 S SB267268 OR SB() (267268 OR 267 268)  
 L21 4 S SB273005 OR SB() (273005 OR 273 005)  
 L22 0 S CP4632 OR CP 4632  
 L23 1 S SH306 OR SH 306  
 L24 4 S SB273005 OR SB() (273005 OR 273 005)  
 L25 0 S SC72115 OR SC() (72115 OR 72 115)

FILE 'REGISTRY' ENTERED AT 11:07:03 ON 14 FEB 2005

L26 13 S 243972-21-6 OR 211308-14-4 OR 243672-10-8 OR 243970-98-1 OR 2  
 L27 2 S 181819-14-7 OR 249298-39-3  
 E C22H27N5O6S/MF  
 L28 1 S E3 AND 46.150.18/RID AND NCNC3/ES AND 3/NR  
 E C24H29N5O6S/MF  
 L29 3 S E3 AND 46.150.18/RID AND NC5/ES AND NOC3-C6/ES AND 4/NR  
 E C19H21N5O4/MF  
 L30 52 S E3 AND 46.150.18/RID AND 2/NR  
 L31 19 S L30 AND AMINOIMINO METHYL  
 L32 8 S L31 AND BETA  
 L33 3 S L32 NOT NC5/ES  
 L34 1 S 188803-61-4  
 E S448/CN  
 E S 448/CN  
 E S-448/CN  
 E SB 267268/CN  
 E SB-267268/CN  
 E C22H24F3N3O4/MF  
 L35 5 S E3 AND NC5/ES AND C6-NC6/ES AND 3/NR  
 SEL RN 3 4  
 L36 2 S E1-E2  
 E CP 4632/CN  
 E CP-4632/CN  
 E C25H31FN6O5S/MF  
 L37 9 S E3 AND 4/NR AND 46.150.18/RID AND NC5/ES AND NCNC3/ES  
 L38 4 S L37 AND 3 FLUORO  
 SEL RN 1 4  
 L39 2 S E1-E2  
 E SC 72115/CN  
 E SC-72115/CN  
 E C21H21BRCLN5O5/MF  
 L40 4 S E3  
 L41 2 S L40 NOT NITRO  
 E C19H27N5O6/MF  
 L42 34 S E3 AND 46.150.18/RID AND 1/NR  
 L43 3 S L42 AND AMINO IMINO METHYL AMINO  
 L44 2 S L43 AND VALINE  
 L45 1 S 141028-95-7  
 E C22H27N5O3/MF  
 L46 2 S E3 AND 46.150.18/RID AND C6-NC2NC3/ES  
 L47 1 S L46 NOT METHOXY  
 E C25H33N5O6S/MF  
 L48 6 S E3 AND 46.150.18/RID AND NC5/ES AND NOC3/ES AND 3/NR  
 L49 2 S L48 NOT TRIMETHYL  
 E C23H31N7O7/MF  
 E C22H31N7O7/MF  
 L51 1 S NCNC2/ES AND NC2NC2/ES AND 46.150.18/RID AND 3/NR AND 7/N AND  
 L52 1573 S NCNC2/ES AND NC2NC2/ES AND 46.150.18/RID AND 3/NR  
 L53 1236 S L52 AND 1/NC  
 L54 0 S L53 AND BENZOYLOXY  
 L55 100 S L53 AND 4 5 DIHYDRO 1H IMIDAZOL

L56 82 S L55 AND PIPERAZIN?  
 L57 42 S L56 NOT CL/ELS  
 L58 16 S L57 AND O/ELS NOT S/ELS  
 L59 3 S L58 AND 23-25/C  
 E C25H30CLN5O5S/MF  
 L60 2 S E3 AND (NCNC3 AND NC5 AND C6)/ES AND 4/NR  
 L61 2535 S (NCNC3 AND NC5 AND C6)/ES AND 4/NR AND 1/CL AND 1/S  
 L62 0 S L61 AND TETRAHYDROPYRIMIDIN?  
 L63 2531 S L61 AND 46.150.18/RID  
 L64 30 S L63 AND 3 CHLORO 4  
 L65 4 S L64 AND TETRAHYDRO?  
 SEL RN 3 4  
 L66 2 S E1-E2  
 L67 51 S L63 AND TETRAHYDRO? NOT L65  
 L68 24 S L67 AND 3 CHLORO  
 E C22H24F3N3O4/MF  
 L69 5 S E3 AND NC5/ES AND C6-NC6/ES  
 SEL RN 1 2  
 L70 2 S E1-E2  
 L71 36 S L26-L29,L34,L36,L39,L41,L45,L47,L49,L59,L66,L70  
 E LM 609/CN  
 L72 1 S E3 OR VITAXIN/CN  
 E ABCIXIMAB/CN  
 L73 1 S E3  
 E XJ 735/CN  
 L74 1 S E3  
 E XK 002/CN  
 L75 1 S E3  
 E DMP 728/CN  
 L76 1 S E3  
 E SK&F 107260/CN  
 E SK AND F 107260/CN  
 E SK/CN  
 E 107260  
 L77 15 S E3  
 L78 1 S L77 AND 4/SQL  
 E EMD 121974/CN  
 L79 1 S E3

FILE 'HCAPLUS' ENTERED AT 11:59:56 ON 14 FEB 2005

L80 19 S CYCLO RGDFV  
 L81 0 S AS PEN RGDC OH  
 L82 0 S AS PEN RGDC  
 L83 0 S PEN RGDC  
 L84 0 S RGDC OH  
 L85 61 S ?RGDC?  
 L86 36 S L85 NOT ?CRGDC?  
 L87 0 S L86 AND ASPEN?  
 L88 1 S L86 AND ACPEN?  
 L89 1 S L85 AND ACPEN?  
 L90 0 S L85 AND AC PEN?  
 L91 0 S CYCLO RGD MAMB P  
 L92 0 S RGD MAMB  
 L93 1 S RGD(L) MAMB  
 L94 2 S L88,L89,L93  
 SEL RN

FILE 'REGISTRY' ENTERED AT 12:07:38 ON 14 FEB 2005

L95 20 S E1-E20  
 L96 13 S L95 AND CYCLO  
 L97 12 S L96 NOT L72-L76,L78,L79  
 L98 7 S L72-L76,L78,L79  
 L99 43 S L71,L98

SAV L99 HADDADCOMP2/A

FILE 'HCAPLUS' ENTERED AT 12:11:35 ON 14 FEB 2005

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L100      826 S L99
L101      1027 S LM609 OR LM 609 OR VITAXIN OR ABCIXIMAB OR C7E3 OR C7E 3 OR C
L102      1220 S L100,L101,L1-L25
          ACT HADCOMP2ICA/A
          -----
L103(      10)SEA FILE=REGISTRY ABB=ON PLU=ON 208765-45-1 OR 261619-47-0 OR
L104(      1)SEA FILE=REGISTRY ABB=ON PLU=ON 36357-77-4
L105(      10)SEA FILE=REGISTRY ABB=ON PLU=ON 142375-60-8 OR 136286-50-5 OR
L106(      1)SEA FILE=REGISTRY ABB=ON PLU=ON 261619-50-5
L107(      18)SEA FILE=REGISTRY ABB=ON PLU=ON 184036-34-8 OR 215501-47-6 OR
L108(      5)SEA FILE=REGISTRY ABB=ON PLU=ON 154473-03-7 OR 445475-88-7 OR
L109(      1)SEA FILE=REGISTRY ABB=ON PLU=ON "TBC 11251"/CN
L110(      1)SEA FILE=REGISTRY ABB=ON PLU=ON "AC 610612"/CN
L111(      45)SEA FILE=REGISTRY ABB=ON PLU=ON (L103 OR L104 OR L105 OR L106
L112(      42)SEA FILE=REGISTRY ABB=ON PLU=ON (136286-50-5/CRN OR 136553-74
L113(      41)SEA FILE=REGISTRY ABB=ON PLU=ON L112 NOT MXS/CI
L114(      31)SEA FILE=REGISTRY ABB=ON PLU=ON L113 NOT (COMP2 OR WITH)
L115(      76)SEA FILE=REGISTRY ABB=ON PLU=ON (L111 OR L114)
L116      STR
L117(      319)SEA FILE=REGISTRY SSS FUL L116
L118      STR
L119(      4)SEA FILE=REGISTRY SUB=L117 CSS FUL L118
L120(      5)SEA FILE=REGISTRY ABB=ON PLU=ON C27H25NO6/MF AND 46.150.18/RI
L121(      1)SEA FILE=REGISTRY ABB=ON PLU=ON L120 AND DIMETHYLAMINO
L122(      9)SEA FILE=REGISTRY ABB=ON PLU=ON C25H21NO6/MF AND 46.150.18/RI
L123(      2)SEA FILE=REGISTRY ABB=ON PLU=ON L122 AND METHOXY AND AMINOPHE
L124(      1)SEA FILE=REGISTRY ABB=ON PLU=ON L123 AND 3 AMINO
L125(      139)SEA FILE=REGISTRY ABB=ON PLU=ON N4C/ES AND NC5/ES AND NCNC3/E
L126(      27)SEA FILE=REGISTRY ABB=ON PLU=ON L125 AND 9/N AND S/ELS
L127(      7)SEA FILE=REGISTRY ABB=ON PLU=ON L126 AND 6/O
L128(      3)SEA FILE=REGISTRY ABB=ON PLU=ON L127 AND 27/C
L129(      5)SEA FILE=REGISTRY ABB=ON PLU=ON (L128 OR L121 OR L124 OR L128
L130(      85)SEA FILE=REGISTRY ABB=ON PLU=ON (L115 OR L119 OR L129)
L131      STR
L132(      319)SEA FILE=REGISTRY SSS FUL L131
L133(      65)SEA FILE=REGISTRY ABB=ON PLU=ON L132 AND 4 6 DIMETHOXY
L134(      31)SEA FILE=REGISTRY ABB=ON PLU=ON L133 AND 2/N AND 6/O
L135(      4)SEA FILE=REGISTRY ABB=ON PLU=ON L134 AND C22H22N2O6
L136(      68)SEA FILE=REGISTRY ABB=ON PLU=ON L132 AND 2/N AND 6/O
L137(      31)SEA FILE=REGISTRY ABB=ON PLU=ON L136 AND ETHOXY
L138(      29)SEA FILE=REGISTRY ABB=ON PLU=ON L137 AND METHOXY
L139(      6)SEA FILE=REGISTRY ABB=ON PLU=ON L138 AND 4 6 DIMETHYL
L140(      5)SEA FILE=REGISTRY ABB=ON PLU=ON L139 NOT 204267-90-3
L141(      64)SEA FILE=REGISTRY ABB=ON PLU=ON L132 AND 2/N AND 4/O
L142(      34)SEA FILE=REGISTRY ABB=ON PLU=ON L141 AND 4 6 DIMETHYL
L143(      9)SEA FILE=REGISTRY ABB=ON PLU=ON L142 AND METHOXY
L144(      2)SEA FILE=REGISTRY ABB=ON PLU=ON L143 AND C22H22N2O4
L145(      8)SEA FILE=REGISTRY ABB=ON PLU=ON L132 AND 2/N AND 3/O
L146(      2)SEA FILE=REGISTRY ABB=ON PLU=ON L145 AND C22H22N2O3
L147(      13)SEA FILE=REGISTRY ABB=ON PLU=ON (L135 OR L140 OR L144 OR L146
L148(      96)SEA FILE=REGISTRY ABB=ON PLU=ON L130 OR L147
L149(      1627)SEA FILE=HCAPLUS ABB=ON PLU=ON L148
L150(      6)SEA FILE=HCAPLUS ABB=ON PLU=ON CGS31447 OR CGS(W) (31447 OR 31
L151(      3)SEA FILE=HCAPLUS ABB=ON PLU=ON CGS34043 OR CGS(W) (34043 OR 34
L152(      12)SEA FILE=HCAPLUS ABB=ON PLU=ON CGS35066 OR CGS(W) (35066 OR 35
L153(      1)SEA FILE=HCAPLUS ABB=ON PLU=ON CGS35339 OR CGS(W) (35339 OR 35
L154(      12)SEA FILE=HCAPLUS ABB=ON PLU=ON CGS35066 OR CGS(W) (35066 OR 35
L155(      2)SEA FILE=HCAPLUS ABB=ON PLU=ON WS79089A OR WS(W) (79089A OR 79
L156(      3)SEA FILE=HCAPLUS ABB=ON PLU=ON WS75624A OR WS(W) (75624A OR 75
L157(      3)SEA FILE=HCAPLUS ABB=ON PLU=ON PD069185 OR PD(W) (069185 OR 06

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L158 ( 3) SEA FILE=HCAPLUS ABB=ON PLU=ON SCH54470 OR SCH(W) (54470 OR 54  
 L159 ( 0) SEA FILE=HCAPLUS ABB=ON PLU=ON RU69296 OR RU(W) (69296 OR 69 2  
 L160 ( 0) SEA FILE=HCAPLUS ABB=ON PLU=ON RU69739 OR RU(W) (69739 OR 69 7  
 L161 ( 0) SEA FILE=HCAPLUS ABB=ON PLU=ON KC12792(W) (2AB OR 2 AB) OR KC(  
 L162 ( 5) SEA FILE=HCAPLUS ABB=ON PLU=ON SLV306 OR SLV 306  
 L163 ( 17) SEA FILE=HCAPLUS ABB=ON PLU=ON FR901533 OR FR(W) (901533 OR 90  
 L164 ( 0) SEA FILE=HCAPLUS ABB=ON PLU=ON POHOSPHORAMIDON?  
 L165 ( 1373) SEA FILE=HCAPLUS ABB=ON PLU=ON PHOSPHORAMIDON?  
 L166 ( 0) SEA FILE=HCAPLUS ABB=ON PLU=ON BROMOBENZY? (L) SULF? (L) AMINO (L)  
 L167 ( 0) SEA FILE=HCAPLUS ABB=ON PLU=ON BROMOBENZY? (L) SULF? (L) AMINO (L)  
 L168 ( 273) SEA FILE=HCAPLUS ABB=ON PLU=ON FR139317 OR FR(W) (139317 OR 13  
 L169 ( 1) SEA FILE=HCAPLUS ABB=ON PLU=ON FR901367 OR FR(W) (901367 OR 90  
 L170 ( 1) SEA FILE=HCAPLUS ABB=ON PLU=ON BE182578 OR BE(W) (182578 OR 18  
 L171 ( 1454) SEA FILE=HCAPLUS ABB=ON PLU=ON BQ123 OR BQ 123  
 L172 ( 111) SEA FILE=HCAPLUS ABB=ON PLU=ON TAK044 OR TAK 044  
 L173 ( 85) SEA FILE=HCAPLUS ABB=ON PLU=ON PD142893 OR PD(W) (142893 OR 14  
 L174 ( 8) SEA FILE=HCAPLUS ABB=ON PLU=ON PD156252 OR PD(W) (156252 OR 15  
 L175 ( 72) SEA FILE=HCAPLUS ABB=ON PLU=ON BQ485 OR BQ 485  
 L176 ( 4) SEA FILE=HCAPLUS ABB=ON PLU=ON COCHINMICIN# (W) (1 OR I)  
 L177 ( 0) SEA FILE=HCAPLUS ABB=ON PLU=ON MYRICERON? (L) CAFFEIC ACID ES  
 L178 ( 0) SEA FILE=HCAPLUS ABB=ON PLU=ON MYRICERON? (L) CAFFEIC ACID  
 L179 ( 16) SEA FILE=HCAPLUS ABB=ON PLU=ON MYRICERON?  
 L180 ( 4) SEA FILE=HCAPLUS ABB=ON PLU=ON MYRICERON? (L) CAFFEOYL? (L) E  
 L181 ( 5) SEA FILE=HCAPLUS ABB=ON PLU=ON CYCLO(L) TRP(L) GLU(L) ALA(L) ALLO  
 L182 ( 17) SEA FILE=HCAPLUS ABB=ON PLU=ON BE18257B OR BE(W) (18257B OR 18  
 L183 ( 3) SEA FILE=HCAPLUS ABB=ON PLU=ON L181 AND L182  
 L184 ( 22) SEA FILE=HCAPLUS ABB=ON PLU=ON BE18257# OR BE(W) (18257# OR 18  
 L185 ( 3) SEA FILE=HCAPLUS ABB=ON PLU=ON L181 AND L184  
 L186 ( 17) SEA FILE=HCAPLUS ABB=ON PLU=ON (L182 OR L183)  
 L187 ( 31) SEA FILE=HCAPLUS ABB=ON PLU=ON SITAXSENTAN#  
 L188 ( 5) SEA FILE=HCAPLUS ABB=ON PLU=ON TBC3214 OR TBC 3214  
 L189 ( 8) SEA FILE=HCAPLUS ABB=ON PLU=ON TBC3711 OR TBC 3711  
 L190 ( 173) SEA FILE=HCAPLUS ABB=ON PLU=ON SB209670 OR SB(W) (209670 OR 20  
 L191 ( 654) SEA FILE=HCAPLUS ABB=ON PLU=ON BOSENTAN#  
 L192 ( 71) SEA FILE=HCAPLUS ABB=ON PLU=ON PD156707 OR PD(W) (156707 OR 15  
 L193 ( 15) SEA FILE=HCAPLUS ABB=ON PLU=ON "L749329" OR L(W) (749329 OR 74  
 L194 ( 6) SEA FILE=HCAPLUS ABB=ON PLU=ON "L754142" OR L(W) (754 142 OR 7  
 L195 ( 7) SEA FILE=HCAPLUS ABB=ON PLU=ON ENRASENTAN#  
 L196 ( 1) SEA FILE=HCAPLUS ABB=ON PLU=ON A127772 OR A(W) (127772 OR 127  
 L197 ( 104) SEA FILE=HCAPLUS ABB=ON PLU=ON ABTRASENTAN# OR ABT627 OR ABT  
 L198 ( 3) SEA FILE=HCAPLUS ABB=ON PLU=ON EMD94246 OR EMD(W) (94246 OR 94  
 L199 ( 9) SEA FILE=HCAPLUS ABB=ON PLU=ON ZD1611 OR ZD 1611  
 L200 ( 3) SEA FILE=HCAPLUS ABB=ON PLU=ON K8794 OR K 8794  
 L201 ( 24) SEA FILE=HCAPLUS ABB=ON PLU=ON A182086 OR A(W) (182086 OR 182  
 L202 ( 1) SEA FILE=HCAPLUS ABB=ON PLU=ON PD163070 OR PD(W) (163070 OR 16  
 L203 ( 0) SEA FILE=HCAPLUS ABB=ON PLU=ON BENZODIOXOL? (L) DIMETHYLAMINO(L  
 L204 ( 0) SEA FILE=HCAPLUS ABB=ON PLU=ON BENZODIOXOL? (L) METHOXYPHENYL? (L  
 L205 ( 0) SEA FILE=HCAPLUS ABB=ON PLU=ON BENZODIOXOL? (L) BUTENOIC  
 L206 ( 0) SEA FILE=HCAPLUS ABB=ON PLU=ON PD166557 OR PD(W) (166557 OR 16  
 L207 ( 16) SEA FILE=HCAPLUS ABB=ON PLU=ON RO 61 1790  
 L208 ( 25) SEA FILE=HCAPLUS ABB=ON PLU=ON BMS193884 OR BMS(W) (193884 OR  
 L209 ( 9) SEA FILE=HCAPLUS ABB=ON PLU=ON BMS207940 OR BMS(W) (207940 OR  
 L210 ( 2) SEA FILE=HCAPLUS ABB=ON PLU=ON SB209598 OR SB(W) (209598 OR 20  
 L211 ( 1) SEA FILE=HCAPLUS ABB=ON PLU=ON SB209834 OR SB(W) (209834 OR 20  
 L212 ( 2) SEA FILE=HCAPLUS ABB=ON PLU=ON A206377 OR A(W) (206377 OR 206  
 L213 ( 5) SEA FILE=HCAPLUS ABB=ON PLU=ON EMD122801 OR EMD(W) (122801 OR  
 L214 ( 60) SEA FILE=HCAPLUS ABB=ON PLU=ON TEZOSENTAN#  
 L215 ( 0) SEA FILE=HCAPLUS ABB=ON PLU=ON AC 61 0612  
 L216 ( 2) SEA FILE=HCAPLUS ABB=ON PLU=ON 61 0612  
 L217 ( 2) SEA FILE=HCAPLUS ABB=ON PLU=ON RO 61 0612  
 L218 ( 8) SEA FILE=HCAPLUS ABB=ON PLU=ON T0201 OR T 0201  
 L219 ( 19) SEA FILE=HCAPLUS ABB=ON PLU=ON J104132 OR J(W) (104132 OR 104  
 L220 ( 0) SEA FILE=HCAPLUS ABB=ON PLU=ON TBC11252 OR TBS(W) (11252 OR 11

L221( 10)SEA FILE=REGISTRY ABB=ON PLU=ON 208765-45-1 OR 261619-47-0 OR  
 L222( 1)SEA FILE=REGISTRY ABB=ON PLU=ON 36357-77-4  
 L223( 10)SEA FILE=REGISTRY ABB=ON PLU=ON 142375-60-8 OR 136286-50-5 OR  
 L224( 1)SEA FILE=REGISTRY ABB=ON PLU=ON 261619-50-5  
 L225( 18)SEA FILE=REGISTRY ABB=ON PLU=ON 184036-34-8 OR 215501-47-6 OR  
 L226( 5)SEA FILE=REGISTRY ABB=ON PLU=ON 154473-03-7 OR 445475-88-7 OR  
 L227( 1)SEA FILE=REGISTRY ABB=ON PLU=ON "TBC 11251"/CN  
 L228( 1)SEA FILE=REGISTRY ABB=ON PLU=ON "AC 610612"/CN  
 L229( 45)SEA FILE=REGISTRY ABB=ON PLU=ON (L221 OR L222 OR L223 OR L224  
 L230( 42)SEA FILE=REGISTRY ABB=ON PLU=ON (136286-50-5/CRN OR 136553-74  
 L231( 41)SEA FILE=REGISTRY ABB=ON PLU=ON L230 NOT MXS/CI  
 L232( 31)SEA FILE=REGISTRY ABB=ON PLU=ON L231 NOT (COMPD OR WITH)  
 L233( 76)SEA FILE=REGISTRY ABB=ON PLU=ON (L229 OR L232)  
 L234( 1463)SEA FILE=HCAPLUS ABB=ON PLU=ON L233  
 L235( 4135)SEA FILE=HCAPLUS ABB=ON PLU=ON (L150 OR L151 OR L152 OR L153  
 L236( 4325)SEA FILE=HCAPLUS ABB=ON PLU=ON (L234 OR L235)  
 L237 STR  
 L238( 319)SEA FILE=REGISTRY SSS FUL L237  
 L239 STR  
 L240( 4)SEA FILE=REGISTRY SUB=L238 CSS FUL L239  
 L241( 9)SEA FILE=HCAPLUS ABB=ON PLU=ON L240  
 L242( 3)SEA FILE=HCAPLUS ABB=ON PLU=ON BSF302146 OR BSF(W) (302146 OR  
 L243( 4329)SEA FILE=HCAPLUS ABB=ON PLU=ON (L236 OR L241 OR L242)  
 L244( 5)SEA FILE=REGISTRY ABB=ON PLU=ON C27H25NO6/MF AND 46.150.18/RI  
 L245( 1)SEA FILE=REGISTRY ABB=ON PLU=ON L244 AND DIMETHYLAMINO  
 L246( 9)SEA FILE=REGISTRY ABB=ON PLU=ON C25H21NO6/MF AND 46.150.18/RI  
 L247( 2)SEA FILE=REGISTRY ABB=ON PLU=ON L246 AND METHOXY AND AMINOPHE  
 L248( 1)SEA FILE=REGISTRY ABB=ON PLU=ON L247 AND 3 AMINO  
 L249( 139)SEA FILE=REGISTRY ABB=ON PLU=ON N4C/ES AND NC5/ES AND NCNC3/E  
 L250( 27)SEA FILE=REGISTRY ABB=ON PLU=ON L249 AND 9/N AND S/ELS  
 L251( 7)SEA FILE=REGISTRY ABB=ON PLU=ON L250 AND 6/O  
 L252( 3)SEA FILE=REGISTRY ABB=ON PLU=ON L251 AND 27/C  
 L253( 5)SEA FILE=REGISTRY ABB=ON PLU=ON (L252 OR L245 OR L248 OR L252  
 L254( 54)SEA FILE=HCAPLUS ABB=ON PLU=ON L253  
 L255( 4332)SEA FILE=HCAPLUS ABB=ON PLU=ON (L254 OR L243)  
 L256( 4447)SEA FILE=HCAPLUS ABB=ON PLU=ON (L149 OR L255)  
 L257( 2)SEA FILE=HCAPLUS ABB=ON PLU=ON AC610612 OR AC(W) (610612 OR 61  
 L258 4447 SEA FILE=HCAPLUS ABB=ON PLU=ON (L256 OR L257)  
 -----  
 L259 8 S L102 AND L258  
 L260 29925 S L102 OR INTEGRIN  
 L261 18859 S L258 OR ENDOTHELIN?

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 L309 18859 S L261 OR L308  
 L310 196 S L260 AND L309  
 L311 83 S L310 AND (PY<=2000 OR PRY<=2000 OR AY<=2000)  
 L312 20 S L311 AND (ALPHAV OR ALPHA5 OR ALPHA() (V OR 5))  
 L313 27 S L311 AND (BETA3 OR BETAI3 OR BETA() (3 OR III))  
 L314 14 S L312 AND L313

FILE 'REGISTRY' ENTERED AT 12:21:34 ON 14 FEB 2005

L315 1 S 116243-73-3

FILE 'HCAPLUS' ENTERED AT 12:21:50 ON 14 FEB 2005

L316 18859 S L315 OR L261 OR L309  
 L317 14 S L316 AND L314  
 L318 14 S L317 AND ENDOTHELIN  
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 L319 2 S L318 AND E21-E26

=> fil hcaplus

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FILE COVERS 1907 - 14 Feb 2005 VOL 142 ISS 8  
FILE LAST UPDATED: 13 Feb 2005 (20050213/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d l319 all tot

L319 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:265276 HCAPLUS

DN 134:261258

ED Entered STN: 13 Apr 2001

TI Inhibitors of the **endothelin** signaling pathway and .  
**alpha.v.beta.3 integrin**  
receptor antagonists for combination therapy

IN Amberg, Wilhelm; Kling, Andreas; Hornberger, Wilfried

PA BASF A.-G., Germany

SO PCT Int. Appl., 23 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K045-06

CC 1-8 (Pharmacology)

Section cross-reference(s): 63

FAN.CNT 9

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	RW:			GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG		
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	EP 1227847	A2	20020807	EP 2000-969395	20001002 <--	
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	DE 1999-19962998	A	19991224	<--		
	DE 2000-10027514	A	20000606	<--		
	DE 2000-10028575	A	20000614	<--		
	DE 2000-10039998	A	20000811	<--		
	WO 2000-EP9671	W	20001002	<--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2001024827	ICM	A61K045-06



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C07D333/38; C07D409/12+333B+213; C07D413/12+23B+213;  
C07D417/12+277B+213; C07K005/02A <--

DE 19962998 ECLA A61K045/06; C07D239/34; C07D401/04+241+213;  
C07D401/12+239B+211; C07D401/12+239B+213;  
C07D401/1+239B+213+211; C07D401/14+239B+235C+211;  
C07D401/14+239B+235C+213; C07D401/14+239B+239B+211;  
C07D403/12+239B+233; C07D403/12+239B+235C;  
C07D403/12+241+239B; C07D403/1+243+239B;  
C07D403/14+243+239B+207; C07D405/04+309+239C;  
C07D405/14+309+239B+213; C07D405/14+30+239B+233;  
C07D405/14R+309+239B+213+211;  
C07D405/14R+309+241+239B+213; C07D409/14+333B+239B+213;  
C07D409/14+333B+239B+235C; C07D417/12+277B+239B;  
C07D417/14+277B+239B+235C; C07D417/14+309+277B213 <--

DE 10027514 ECLA A61K045/06 <--

DE 10028575 ECLA A61K045/06 <--

DE 10039998 ECLA A61K045/06 <--

AB An **endothelin** blocker is used in combination with an .  
**alpha.v.beta.3 integrin**  
receptor antagonist for the treatment or prevention of diseases. The  
invention particularly discloses the use of a pharmaceutical composition  
comprising an **endothelin** blocker and an  $\alpha$   
**v.beta.3 integrin** receptor  
antagonist, for the treatment or prevention of cardiovascular disorders,  
particularly for the treatment or prevention of restenosis after vessel  
injury or revascularization treatment. The pharmaceutical composition itself  
is also disclosed.

ST cardiovascular therapeutic **endothelin** blocker **integrin**  
antagonist; **alphav beta3 integrin** antagonist  
**endothelin** blocker therapeutic; restenosis **endothelin**  
blocker **integrin** antagonist; revascularization  
**endothelin** blocker **integrin** antagonist

IT Cardiovascular agents  
Drug delivery systems  
(**endothelin** signaling pathway inhibitors and  $\alpha$   
**v $\beta$  3 integrin** receptor  
antagonists for combination therapy)

IT **Endothelin** receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(**endothelin** signaling pathway inhibitors and  $\alpha$   
**v $\beta$  3 integrin** receptor  
antagonists for combination therapy)

IT Blood vessel, disease  
(injury; **endothelin** signaling pathway inhibitors and  
 $\alpha$  **v $\beta$  3 integrin**  
receptor antagonists for combination therapy)

IT Artery, disease  
(restenosis; **endothelin** signaling pathway inhibitors and  
 $\alpha$  **v $\beta$  3 integrin**  
receptor antagonists for combination therapy)

IT Blood vessel  
(revascularization; **endothelin** signaling pathway inhibitors  
and  $\alpha$  **v $\beta$  3**  
**integrin** receptor antagonists for combination therapy)

IT **Integrins**  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
( $\alpha$  **v $\beta$  3**;  
**endothelin** signaling pathway inhibitors and  $\alpha$   
**v $\beta$  3 integrin** receptor  
antagonists for combination therapy)

IT 116243-73-3, **Endothelin**  
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(**endothelin** signaling pathway inhibitors and  $\alpha$   
 $v\beta$  3 **integrin** receptor  
 antagonists for combination therapy)

L319 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1997:624952 HCAPLUS  
 DN 127:288569  
 ED Entered STN: 01 Oct 1997  
 TI RGDN peptide interaction with endothelial **.alpha.5**  
 $\beta$ 1 **integrin** causes sustained **endothelin**-dependent  
 vasoconstriction of rat skeletal muscle arterioles  
 AU Mogford, Jon E.; Davis, George E.; Meininger, Gerald A.  
 CS Microcirculation Research Institute and Department of Medical Physiology,  
 Texas A&M University Health Science Center, Texas AandM University,  
 College Station, TX, 77843-1114, USA  
 SO Journal of Clinical Investigation (1997), 100(6), 1647-1653  
 CODEN: JCINAO; ISSN: 0021-9738  
 PB Rockefeller University Press  
 DT Journal  
 LA English  
 CC 2-10 (Mammalian Hormones)  
 AB The ability of an **integrin**-binding Arg-Gly-Asp-Asn (RGDN)-containing  
 peptide to influence vascular tone by interacting with the **.alpha**  
**.5.beta.1 integrin** was studied using rat skeletal  
 muscle arterioles. After blockade of **.beta.3**  
**integrin** function, isolated arterioles with spontaneous tone  
 showed concentration-dependent vasoconstrictions to topical application of  
 GRGDNP, a peptide that shows a greater ability to interact with **.**  
**alpha.5.beta.1** than with **.alpha.v**.  
**beta.3**. The constriction to GRGDNP (2.1 mM) was  
 inhibited by blocking **.alpha.5 integrin**  
 function, and was intensified by blocking **.beta.3**  
**integrin** function. In contrast, GRGDSP, a peptide that interacts  
 better with **.alpha.v.beta.3**, was  
 unable to induce sustained constrictions. Removal of the endothelium  
 abolished the vasoconstriction in response to GRGDNP, suggesting that the  
 response was due to release of an endothelium-dependent factor. Indeed,  
 blockade of ETA **endothelin** receptors with BQ-610 (1  $\mu$ M),  
 similar to removal of the endothelium and **.alpha.5**  
**integrin** blockade, inhibited the vasoconstriction. These data  
 indicate that interaction of RGD peptides, and in particular the RGDN  
 sequence with endothelial cell **.alpha.5.beta.1**, causes  
**endothelin**-mediated arteriolar vasoconstriction. These results  
 indicate that **integrins** are novel signaling receptors within the  
 vascular wall that affect vasomotor tone, and may play an important role  
 in vascular control.  
 ST RGDN peptide **alpha5beta1 integrin endothelin**  
 vasoconstriction  
 IT **Endothelin** receptors  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL  
 (Biological study); PROC (Process)  
 (ETA; RGDN peptide interaction with endothelial  $\alpha$   
**5.beta.1 integrin** causes **endothelin**  
 -dependent vasoconstriction of rat skeletal muscle arterioles)  
 IT Signal transduction, biological  
 Vasoconstriction  
 (RGDN peptide interaction with endothelial  $\alpha$  5  
 $\beta$ 1 **integrin** causes **endothelin**-dependent  
 vasoconstriction of rat skeletal muscle arterioles)  
 IT Artery  
 (arteriole; RGDN peptide interaction with endothelial  $\alpha$   
**5.beta.1 integrin** causes **endothelin**  
 -dependent vasoconstriction of rat skeletal muscle arterioles)

IT **Integrins**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 ( $\alpha$  5.beta.1; RGDN peptide interaction with endothelial  $\alpha$  5.beta.1 **integrin** causes **endothelin**-dependent vasoconstriction of rat skeletal muscle arterioles)

## IT 114681-65-1, GRGDNP

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (RGDN peptide interaction with endothelial  $\alpha$  5  $\beta$ 1 **integrin** causes **endothelin**-dependent vasoconstriction of rat skeletal muscle arterioles)

IT 116243-73-3, **Endothelin**

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (RGDN peptide interaction with endothelial  $\alpha$  5  $\beta$ 1 **integrin** causes **endothelin**-dependent vasoconstriction of rat skeletal muscle arterioles)

RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD  
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CR 2001-015695 [02]; 2001-081541 [10]; 2001-102208 [11]; 2001-316158 [33];  
 2002-154548 [20]; 2002-216758 [27]; 2002-382639 [41]; 2002-599230 [64]

DNC C2001-089028

TI Use of **endothelin** blockers in combination with **alpha-v-beta-3 integrin** receptor  
 antagonists for the treatment of cardiovascular disease, especially  
 restenosis.

DC B04 B05

IN GENESTE, H; GRAEF, C I; HORNBERGER, W; KLING, A; LANGE, U; LAUTERBACH, A;  
 SEITZ, W; SUBKOWSKI, T; AMBERG, W

PA (BADI) BASF AG

CYC 95

PI WO 2001024827 A2 20010412 (200130)\* EN 22 A61K045-06 <--

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 ICS A61K031-55; A61K045-00; A61P009-00; A61P009-08; C07D211-26;  
 C07D227-04; C07D247-00; C07D277-28; C07D401-04; C07D403-12;  
 C07D405-12; C07D409-04; C07D409-12; C07D417-04; C07D471-04;  
 C07D487-04; C07D495-04  
 AB WO 200124827 A UPAB: 20031030  
 NOVELTY - Use of an **endothelin** blocker in combination with an  
**alpha v beta 3 integrin**  
 receptor antagonist for the manufacture of medicaments for the treatment  
 or prevention of diseases, is new.  
 DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a  
 trade package, comprising (as the active agent) an **endothelin**  
 blocker and/or an **alpha v beta 3**  
**integrin** receptor antagonist with instruction for use of these  
 agents for simultaneous, separate or temporal graduated application for  
 the treatment and/or prevention of disease.  
 ACTIVITY - Cardiovascular.  
 No biological data is given.  
 MECHANISM OF ACTION - Combined inhibition of **endothelin** and  
**alpha v beta 3 integrin**  
 receptor activity.  
 No biological data is given.  
 USE - The medicaments containing the **endothelin** blocker in  
 combination with an **alpha v beta 3**  
**integrin** receptor antagonist are used for the treatment of  
 cardiovascular disorders, especially restenosis after vessel injury or  
 re-vascularization treatments (claimed). Other Disorders include  
 angioplasty (neointima formation, smooth muscle cell migration and  
 proliferation), myocardial infarction and heart failure.  
 ADVANTAGE - Administration of both the **endothelin** blocker  
 in combination with the **alpha v beta**  
**3 integrin** receptor antagonist, reduce restenosis to a  
 greater degree than one of the 2 treatments alone. For example, the  
 combination of the blocker and receptor antagonist in doses too low to be  
 effective alone, is at least as effective as a high mono-therapy with  
 either agent and has less (potential side effects than one principle  
 alone.  
 Dwg.0/0

FS CPI  
 FA AB; DCN  
 MC CPI: B14-F01; B14-F02; B14-L06  
 ABEX UPTX: 20010603

ADMINISTRATION - The **endothelin** blocker and/or an alpha-v-beta-3 **integrin** receptor antagonist may be administered by simultaneous, separate or temporal graduated application (claimed).

L336 ANSWER 2 OF 2 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2001-015695 [02] WPIX

CR 2001-081541 [10]; 2001-102208 [11]; 2001-290578 [30]; 2001-316158 [33];  
 2002-154548 [20]; 2002-216758 [27]; 2002-382639 [41]; 2002-599230 [64]

DNC C2001-004142

TI New **integrin** receptor ligands, especially **integrin-alpha**  
**beta3** ligands, useful for treating e.g. atherosclerosis,  
 rheumatoid arthritis, restenosis, angioplasty and acute kidney failure.

DC B04 B05

IN GENESTE, H; GRAEF, C I; HORNBERGER, W; KLING, A; LANGE, U; LAUTERBACH, A;  
 SADOWSKI, J; SUBKOWSKI, T; ZECHEL, J; HERGENROEDER, S; HILLEN, H; MARKERT,  
 C O; AMBERG, W

PA (BADI) BASF AG

CYC 93

PI WO 2000061551 A2 20001019 (200102)\* GE 299 C07D000-00 <--  
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL  
 OA PT SD SE SL SZ TZ UG ZW  
 W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ  
 EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK  
 LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI  
 SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

DE 19916719 A1 20001019 (200102) C07D413-12 <--

AU 2000041129 A 20001114 (200108) <--

DE 19962998 A1 20010712 (200140) C07D403-02

EP 1171435 A2 20020116 (200207) GE C07D401-14

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT  
 RO SE SI

NO 2001004961 A 20011107 (200207) C07D000-00

BR 2000009739 A 20020409 (200232) C07D401-14

KR 2001108499 A 20011207 (200236) C07D403-14

SK 2001001410 A3 20020702 (200253) C07D401-14

EP 1227847 A2 20020807 (200259) EN A61K045-06 <--

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL RO  
 SI

CZ 2001003678 A3 20020717 (200260) C07D401-14

CN 1353706 A 20020612 (200262) C07D401-14

JP 2002541243 W 20021203 (200309) 352 C07D239-36

ZA 2001008035 A 20021224 (200309)# 266 C07D000-00

HU 2002003338 A2 20030328 (200333) C07D401-14

MX 2001010232 A1 20020401 (200363) C07D000-00

ADT WO 2000061551 A2 WO 2000-EP2746 20000329; DE 19916719 A1 DE  
 1999-1016719 19990413; AU 2000041129 A AU 2000-41129 20000329  
 ; DE 19962998 A1 DE 1999-1062998 19991224; EP 1171435 A2 EP  
 2000-920612 20000329, WO 2000-EP2746 20000329; NO  
 2001004961 A WO 2000-EP2746 20000329, NO 2001-4961 20011012; BR  
 2000009739 A BR 2000-9739 20000329, WO 2000-EP2746  
 20000329; KR 2001108499 A KR 2001-713063 20011013; SK 2001001410 A3  
 WO 2000-EP2746 20000329, SK 2001-1410 20000329; EP  
 1227847 A2 EP 2000-969395 20001002, WO 2000-EP9671  
 20001002; CZ 2001003678 A3 WO 2000-EP2746 20000329, CZ  
 2001-3678 20000329; CN 1353706 A CN 2000-807554 20000329;  
 JP 2002541243 W JP 2000-610827 20000329, WO 2000-EP2746  
 20000329; ZA 2001008035 A ZA 2001-8035 20011001; HU 2002003338 A2  
 WO 2000-EP2746 20000329, HU 2002-3338 20000329; MX  
 2001010232 A1 WO 2000-EP2746 20000329, MX 2001-10232 20011010

FDT AU 2000041129 A Based on WO 2000061551; EP 1171435 A2 Based on WO 2000061551; BR 2000009739 A Based on WO 2000061551; SK 2001001410 A3 Based on WO 2000061551; EP 1227847 A2 Based on WO 2001024827; CZ 2001003678 A3 Based on WO 2000061551; JP 2002541243 W Based on WO 2000061551; HU 2002003338 A2 Based on WO 2000061551; MX 2001010232 A1 Based on WO 2000061551

PRAI DE 1999-19962998 19991224; DE 1999-19916719 19990413; DE 1999-19948269 19991006; DE 2000-10027514 20000606; DE 2000-10028575 20000614; DE 2000-10039998 20000811; ZA 2001-8035 20011001

IC ICM A61K045-06; C07D000-00; C07D239-36; C07D401-14; C07D403-02; C07D403-14; C07D413-12

ICS A61K031-415; A61K031-505; A61K031-506; A61K031-517; A61K031-541; A61K045-00; A61P003-14; A61P007-00; A61P007-02; A61P009-00; A61P009-10; A61P009-12; A61P013-12; A61P017-02; A61P017-06; A61P019-00; A61P019-08; A61P019-10; A61P029-00; A61P031-00; A61P031-04; A61P031-12; A61P033-00; A61P035-00; C07C403-14; C07D239-28; C07D239-32; C07D239-46; C07D239-56; C07D239-60; C07D239-70; C07D401-02; C07D401-06; C07D401-12; C07D403-04; C07D403-06; C07D403-12; C07D405-04; C07D405-14; C07D409-02; C07D409-14; C07D413-14; C07D417-02; C07D417-12; C07D417-14; C07D471-04

AB WO 200061551 A UPAB: 20031001

NOVELTY - **Integrin** receptor ligands (I), their salts, prodrugs, their enantiomers or diastereomers and tautomeres are new.

DETAILED DESCRIPTION - **Integrin** receptor ligands of formula (I), their salts, prodrugs, their enantiomers or diastereomers and tautomeres are new.

L = U-T;

T = COOH or a group hydrolyzable to COOH;

U = (CRL1RL2)a-(VL)b-(CRL3RL4)c-(WL)d-(CRL5RL6)e-(XL)f(CRL7RL8)g;

a, c, e, g = 0-3;

b, d, f = 0 or 1;

RL1-RL8 = e.g. H, halo or OH; (CH2)w-(YL)y-RL9; 3-7C cycloalkyl, aryl, arylalkyl, hetaryl or hetarylalkyl (all optionally substituted); or

RL1+RL2, RL3+RL4, RL5+RL6, RL7+RL8 = 3-7-membered ring optionally substituted and optionally saturated carbo- or heterocyclyl, which may contain up to 3 N, O or S;

w = 0-4,

YL = CO, CON(RY1), N(RY1)CO, N(RY1)-C(O)N(RY1 asterisk), N(RY1)-COO, O, S, SO2, SO2N(RY1), SO2O, COO, OCO, OCON(RY1), N(RY1) or N(RY1')SO2;

RY1, RY1 asterisk = e.g. H, optionally substituted 1-6C alkyl or SO2-1-6C alkyl or optionally substituted, CO-aryl, SO2-ary-, hetaryl, CO-hetaryl or SO2-alkylene-aryl;

RL9 = e.g. H, OH, CN, halo, optionally substituted 1-6C alkyl, Cl substituted 1-4C-alkyl or aryl substituted alkynyl or alkenyl, optionally substituted 6-12C-bicycloalkyl; or

RL9+RY1, RL9+RY1 asterisk = optionally unsaturated 3-7-heterocyclyl optionally containing up to 3 O, S or N;

WL = optionally substituted 4-11-membered mono- or polycyclic aliphatic or aromatic hydrocarbonyl, having up to 6 double bonds and up to 6 N, O, S;

VL, XL = CO, CONRL10, NRL10CO, SO, SO2, SO2NRL10, NRL10SO2, CS, CSNRL10, NRL10CS, CSO, OCS, COO, OCO, O, ethynylene, CHRL11OCHRL12, C(=CRL11RL12), CRL11=CRL12, CRL11(ORL13)-CHRL12, CHRL11-CRL12(ORL13), CH(NRL14SO2RL15), -CH(NRL14CORL15), CH(NRL14COORL16), CH(NRL14CONRL14'CRL15), CH(CORL15), CH(COORL16) or CH(CONRL14RL15);

RL10 = e.g. H, optionally substituted 1-6C-alkyl, 1-6C-alkoxyalkyl, 2-6C alkenyl, 3-12C alkynyl; or

RL10 and RL1, RL 2, RL 3, RL 4, RL5, RL6, RL7 or RL8 together form an optionally substituted 4-8 membered heterocyclyl, containing up to 5 O, N or S;

RL11, RL12 = e.g. H, OH, 1-6C alkyl or alkylene-cycloalkyl or optionally substituted 3-7C cycloalkyl, aryl, arylalkyl, hetaryl or hetarylalkyl;

RL13 = e.g. H, optionally substituted 1-6C alkyl or alkylene-cycloalkyl or optionally substituted 3-7C-cycloalkyl or hetarylalkyl;

RL14, RL14' = e.g. H, optionally substituted 1-6C alkyl, 1-6C alkoxyalkyl, 2-6C alkenyl, 3-12C alkynyl, CO-1-6C alkyl, CO-O-1-6C-alkyl-, 1-6C-alkylene-3-7C-cycloalkyl or SO<sub>2</sub>-1-6C-alkyl or optionally substituted 3-7C cycloalkyl;

RL15 = optionally substituted 1-6C-alkyl, alkoxyalkyl, 1-6C-alkylene-3-7C-cycloalkyl, 6-12C-bicycloalkyl, 1-6C-alkylene-6-12C-bicycloalkyl, 7-20C tricycloalkyl or 1-6C alkylene-7-20C tricycloalkyl, up to 3 substituted 3-7C cycloalkyl, aryl, arylalkyl, hetarylalkyl or 3-8-membered optionally saturated or aromatic heterocyclyl; or

RL15+RL14, RL15+RL14 asterisk = an optionally saturated 3-7C heterocyclyl, optionally containing up to 2 O, S or N;

RL16 = optionally substituted 1-6C-alkyl, alkoxyalkyl or 1-6C-alkylene-3-7C cycloalkyl or optionally substituted 3-7C cycloalkyl, aryl, arylalkyl, hetaryl or hetarylalkyl,

G = a group of formula (a);

the incorporation of G can be any of the 2 orientations;

ZG = O, S or NRG<sub>3</sub>;

RG<sub>1</sub>, RG<sub>2</sub> = H, CN, NO<sub>2</sub>, halo, optionally substituted 1-6C alkyl, 2-6C alkenyl or 2-6C alkynyl, optionally substituted 1-4C alkylene-ORG<sub>4</sub>, 1-4C-alkylene-CO-ORG<sub>4</sub>, 1-4C-alkylene-CO-RG<sub>4</sub>, 1-4C-alkylene-SO<sub>2</sub>-NRG<sub>5</sub>RG<sub>6</sub>, 1-4C-alkylene-CO-NRG<sub>5</sub>RG<sub>6</sub>, 1-4C-alkylene-NRG<sub>5</sub>RG<sub>6</sub> or 1-4C-alkylene-SRG<sub>4</sub>, optionally substituted 3-7C-cycloalkyl, 1-4C-alkylene-3-7C cycloalkyl, 1-4C alkylene-3-7C-heterocycloalkyl or 1-4C-alkylene-3-7C heterocycloalkenyl, optionally substituted aryl, arylalkyl, hetaryl or hetarylalkyl, SRG<sub>4</sub>, ORG<sub>4</sub>, SORG<sub>4</sub>, SO<sub>2</sub>-RG<sub>4</sub>, COORG<sub>4</sub>, OCORG<sub>4</sub>, O-CO-NRG<sub>5</sub>RG<sub>6</sub>, SO<sub>2</sub>NRG<sub>5</sub>RG<sub>6</sub>, CONRG<sub>5</sub>RG<sub>6</sub>, NRG<sub>5</sub>RG<sub>6</sub> or CORG<sub>4</sub>; or

RG<sub>1</sub>+RG<sub>2</sub> = optionally substituted optionally saturated or aromatic 3-9-membered carbocyclyl, carbopolycyclyl, heterocyclyl or heteropolycyclyl, containing up to 4 O, N or S;

RG<sub>3</sub> = H, OH, CN, optionally substituted 1-6C alkyl or 1-4C-alkoxy or optionally substituted 3-7C-cycloalkyl, O-3-7C-cycloalkyl, aryl, -O-aryl, arylalkyl-or O-alkylene-aryl;

RG<sub>4</sub> = e.g. H, optionally substituted 1-8C alkyl or optionally substituted aryl or heterocycloalkyl;

RG<sub>5</sub>, RG<sub>6</sub> = e.g. H, optionally substituted 1-8C alkyl or SO<sub>2</sub>RG<sub>4</sub>, COORG<sub>4</sub>, CONRG<sub>4</sub>RG<sub>4</sub> asterisk or CORG<sub>4</sub>;

RG<sub>4</sub> asterisk = as for RG<sub>4</sub>;

B = a structural element containing at least one atom which can act as a hydrogen acceptor under physiological conditions, where at least one hydrogen acceptor atom along the shortest possible path on the structural element frame is at a distance of 4-13 atomic bonds to the structural element G.

The full definitions are given in the DEFINITIONS (Full Definitions) Field.

INDEPENDENT CLAIMS are also included for the following:

(1) use of structural elements of formula -G-L for the preparation of compounds which bind to integrin receptors;

(2) pharmaceuticals containing -G-L;

(3) use of (I) in the manufacture of medicaments for treating diseases, especially diseases involving excessive or reduced interaction between integrins (particularly alpha v beta 3-integrin) and their natural ligands;

(4) pharmaceutical composition containing (I), optionally auxiliary substances and at least a further compound selected from other active substances, and the use of these compositions for treating specific diseases.

ACTIVITY - Antiarteriosclerotic; antirheumatic; antiarthritic;



vasotropic; nephrotropic; antithrombotic; cardiant; cerebroprotective; cytostatic; osteopathic; hypotensive; antipsoriatic; virucide; protozoacide; antibacterial; antiinflammatory; vulnerary.

MECHANISM OF ACTION - Integrin receptor ligands, especially integrin-alpha v beta 3 ligands.

An alpha v beta 3 assay is described based on the competition between the natural integrin- alpha v beta 3 ligand, vitronectin, and (I) for the binding to solid phase bound integrin- alpha v beta 3 but no results are given.

USE - (I) are useful as integrin-receptor ligands, especially as ligands of the alpha v beta 3-integrin receptor for treating atherosclerosis, rheumatoid arthritis, restenosis after vessel damage or stent implantation, angioplasty, acute kidney failure, angiogenesis-associated microangiopathy, diabetic angiopathy, platelet-mediated vascular closure, arterial thrombosis, congestive heart failure, myocardial infarct, stroke, cancer, osteoporosis, hypertension, psoriasis or viral, parasitic or bacterial diseases, inflammation, wounds, hyperparathyroidism, Paget's disease, malignant hypercalcemia, or metastatic osteolytic lesions (all claimed).

Dwg.0/0

FS CPI

FA AB; GI; DCN

MC CPI: B06-H; B07-D12; B14-A01; B14-A02; B14-B02; B14-C03; B14-C06; B14-C09B; B14-F01; B14-F02B; B14-F02D; B14-F04; B14-F07; B14-H01; B14-N01; B14-N10; B14-N16; B14-N17B; B14-N17C

TECH UPTX: 20010110

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Compositions: In (4), the following are claimed:

(5) pharmaceutical composition containing (I), optionally auxiliary substances and at least a further compound selected from: (i) inhibitors of platelet adhesion, activation or aggregation; (ii) anticoagulant which prevent thrombin activation or formation; and (iii) antagonists of platelet activating compounds or selectin antagonists;

(6) use of the composition in (5) for the preparation of a medicament for treating platelet mediated vascular closure or thrombosis;

(7) pharmaceutical composition containing at least one compound (I), optionally an auxiliary substances, and at least one further compound selected from: (a) inhibitors of platelet activation or aggregation; (b) serin-protease inhibitors; (c) compounds for reducing fibrinogen levels; (d) selectin antagonists; (e) antagonists of ICAM-1 or VCAM-1; (f) inhibitors of leukocyte adhesion; (g) inhibitors of vessel wall transmigration; (h) fibrinolysis-modulating compounds; (i) inhibitors of complement factors; (j) **endothelin** receptor antagonists; (k) tyrosinase inhibitors; (l) antioxidants; and (m) interleukin 8 antagonists;

(8) use of the composition in (7) for the preparation of medicament for treating myocardial infarct or stroke;

(9) a pharmaceutical composition containing at least one compound (I), optionally auxiliary substances and at least one further compound selected from: (a') **endothelin** antagonists; (b') ACE inhibitors; (c') angiotensin receptor antagonists; (d') endopeptidase inhibitors; (e') beta-blockers; (f') calcium channel antagonists; (g') phosphodiesterase inhibitors; and (h') caspase inhibitors;

(10) use of the composition in (9) for the preparation of a medicament for treating congestive heart failure;

(11) a pharmaceutical composition containing at least one compound (I), optionally auxiliary substances and at least one further compound selected from: (a'') thrombin inhibitors; (b'') inhibitors of factor Xa; (c'') inhibitors of the coagulation pathway leading to thrombin formation; (d'') inhibitors of platelet adhesion, activation or aggregation; (e'') **endothelin** receptor antagonists; (f'') nitrogen oxide synthase inhibitors; (g'') CD44 antagonists; (h'') selectin antagonists; (i'') MCP-1 antagonists; (j'') inhibitors of signal transduction in

proliferating cells; (k'') antagonists of cell response mediated by EGF, PDGF, VEGF or bFGF; and (l'') antioxidants;

(12) use of the composition in (11) for the preparation of a medicament for treating restenosis after vessel damage or stent implant;

(13) a pharmaceutical composition containing at least one compound (I), optionally auxiliary substances and at least one further compound selected from: (a1) antagonist of cell response mediated by EGF, PDGF, VEGF or bFGF; (a2) heparin or low molecular heparins or other GAG's; (a3) inhibitors of MMP's; (a4) selectin antagonist; (a5) **endothelin** antagonist; (a6) ACE inhibitors; (a7) angiotensin receptor antagonists; (a8) glycosylation inhibitors; or (a9) AGE-formation inhibitors or AGE-breakers and antagonists of their receptors;

(14) use of the composition in (13) for the preparation of a medicament for treating diabetic angiopathy;

(15) a pharmaceutical composition containing at least one compound (I), optionally auxiliary substances and at least one further compound selected from: (b1) fat lowering compounds; (b2) selectin antagonists; (b3) antagonists of ICAM or VCAM-1; (b4) heparin or low molecular heparins or further GAG's; (b5) inhibitors of MMP's; (b6) **endothelin** antagonists; (b7) apolipoprotein A1-antagonists; (b8) cholesterol antagonists; (b9) HMG-CoA reductase inhibitors; (b10) ACAT inhibitors; (b11) ACE inhibitors; (b12) angiotensin receptor antagonists; (b13) tyrosine kinase inhibitors; (b14) protein kinase C inhibitors; (b15) calcium channel antagonists; (b16) LDL-receptor function stimulants; (b17) antioxidants; (b18) LCAT mimetics; and (b19) free radical scavengers;

(16) use of the composition in (15) for the preparation of a medicament for treating atherosclerosis;

(17) a pharmaceutical composition containing at least one compound (I), optionally auxiliary substances and at least one further compound selected from: (c1) cytostatic or neoplastic compounds; (c2) compounds which inhibit proliferation; and (c3) heparin or low molecular heparins or other GAG's;

(18) use of the composition in (17) for the preparation of a medicament for treating cancer;

(19) a pharmaceutical composition containing at least one compound (I), optionally auxiliary substances and at least one further compound selected from: (d1) compounds for anti-resorptive therapy; (d2) compounds for hormone exchange therapy; (d3) recombinant human growth hormone; (d4) bisphosphonate; (d5) compounds for calcitonin therapy; (d6) calcitonin stimulants; (d7) calcium channel antagonists; (d8) bone formation stimulants; (d9) interleukin 6-antagonists; or (d10) src tyrosinase inhibitors;

(20) use of the composition in (19) for the preparation of a medicament for treating osteoporosis;

(21) a pharmaceutical composition containing at least one compound (I), optionally auxiliary substances and at least one further compound selected from: (e1) TNF antagonists; (e2) antagonists of VLA-4 or VCAM-1; (e3) antagonist of LFA-1, Mac-1 or ICAMs; (e4) complement inhibitors; (e5) immunosuppressives; (e6) interleukin 1, 3 or 8-antagonists; and (e7) dihydrofolate reductase inhibitors;

(22) use of the composition in (21) for the preparation of a medicament for treating rheumatoid arthritis;

(23) a pharmaceutical composition containing at least one compound (I), optionally auxiliary substances and at least one further compound selected from: (f1) collagenase; (f2) PDGF antagonists; and (f3) MMP's;

(24) use of the composition in (22) for the preparation of a medicament for improving wound-healing.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: (I) are prepared e.g. by converting 4-thioxo-3,4-dihydropyrimidin-2(1H)-ones of formula (II) into the corresponding sulfanylacetonitriles of formula (IVb) which are then converted with thioles of formula A-E'-SH to compounds of formula (Vb). Removal of the protecting group leads to compounds of formula (I'). The preparation is preferably performed in the solid phase.

SG1 = protecting group;

E' = as for E but without the (UE)h linkage.

ABEX

UPTX: 20010110

SPECIFIC COMPOUNDS - 15154 Compounds (I) are disclosed, e.g.

4-(((1-((2S)-2-(((benzyloxy)carbonyl)amino)-2-carboxyethyl)-5-methyl-2-oxo-1,2-dihydropyrimidin-4-yl)amino)methyl)-1-pyridin-2-ylpiperidinium acetate (1a).

ADMINISTRATION - Administration is e.g. oral, parenteral, as a spray through the nose-throat area or may be brought in direct contact with the affected tissue. Daily dosage is 0.5-50 mg/kg orally or 0.1-10 mg/kg parenterally.

EXAMPLE - 1.5 g Z-Dap(Fmoc)-2-Cl-tritylresin (substitution: 0.4 mmol/g resin) were treated for 20 minutes with piperidine in DMF (50%). After washing with DMF (5 x 1 minute), the resin was suspended in DMF (6 ml), 2-(N-carbethoxythiocarbamoyl)-1-(N-piperidino)-3-propene added and incubated at room temperature overnight. The mixture was washed with DMF, MeOH and CH<sub>2</sub>Cl<sub>2</sub> and NMP. The resin suspension in NMP (4.5 ml) was treated with Cs<sub>2</sub>CO<sub>3</sub> (1.83 g) in H<sub>2</sub>O (0.89 ml) and a 5 M BrCN solution in MeCN (0.56 ml). After 6 hours' incubation at room temperature, the mixture was filtered under vacuum, and washed with NMP and CH<sub>2</sub>Cl<sub>2</sub>. The obtained resin (0.037 mmol) was suspended in NMP (3.5 ml) and after addition of DIPEA (27 microl) was treated with (1-pyridin-2-yl-piperidin-4-yl)methane amine. The mixture was incubated overnight, filtered under vacuum and washed with DMF, H<sub>2</sub>O, DMF, CH<sub>2</sub>Cl<sub>2</sub>, MeOH and CH<sub>2</sub>Cl<sub>2</sub>. Removal of the product from the resin was conducted with tnfluoroethanol/ethyl acetate/CH<sub>2</sub>Cl<sub>2</sub> at room temperature for 1 hour. The mixture was filtered, evaporated, and the residue taken in 2 ml ethyl acetate and lyophilized to give 22 mg 4-(((1-((2S)-2-(((benzyloxy)carbonyl)amino)-2-carboxyethyl)-5-methyl-2-oxo-1,2-dihydropyrimidin-4-yl)amino)methyl)-1-pyridin-2-ylpiperidinium acetate (1a).

Z-Dap = a group of formula (x).

DEFINITIONS - Full Definitions:

**Integrin** receptor ligands of formula (I), their salts, prodrugs, their enantiomers or diastereomers and tautomeres are new.

L = U-T;

T = COOH or a group hydrolyzable to COOH;

U = (CRL1RL2)a-(VL)b-(CRL3RL4)c-(WL)d-(CRL5RL6)e-(XL)f(CRL7RL8)g;

a, c, e, g = 0-3;

b, d, f = 0 or 1;

RL1-RL8 = H, halo or OH; optionally substituted 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl or 1-6C alkylene-3-7C cycloalkyl; (CH<sub>2</sub>)<sub>w</sub>-(YL)<sub>y</sub>-RL9; 3-7C cycloalkyl, aryl, arylalkyl, hetaryl or hetarylalkyl (all optionally substituted); or

RL1+RL2, RL3+RL4, RL5+RL6, RL7+RL8 = 3-7-membered ring optionally substituted and optionally saturated carbo- or heterocyclyl, which may contain up to 3 N, O or S;

w = 0-4,

YL = CO, CON(RY1), N(RY1)CO, N(RY1)-C(O)N(RY1asterisk), N(RY1)-COO, O, S, SO<sub>2</sub>, SO<sub>2</sub>N(RY1), SO<sub>2</sub>O, COO, OCO, OCON(RY1), N(RY1) or N(RY1')SO<sub>2</sub>;

RY1, RY1asterisk = H, optionally substituted 1-6C alkyl, 1-6C alkoxyalkyl, 2-6C alkenyl, 3-12C alkynyl, CO-alkyl-, COO-alkyl or SO<sub>2</sub>-1-6C alkyl or optionally substituted 3-7C cycloalkyl, aryl, arylalkyl, CO-O-alkylene-aryl, CO-alkylene-aryl, CO-aryl, SO<sub>2</sub>-ary-, hetaryl, CO-hetaryl or SO<sub>2</sub>-alkylene-aryl;

RL9 = H, OH, CN, halo, optionally substituted 1-6C alkyl, 3-7C-cycloalkyl, aryl, heteroaryl or arylalkyl, Cl substituted 1-4C-alkyl or aryl substituted alkynyl or alkenyl, optionally substituted 6-12C-bicycloalkyl, 1-6C alkylene-6-12C-bicycloalkyl-, 7-20C tricycloalkyl or 1-6C-alkylene-7-20C-tricycloalkyl, or 3-8-membered, optionally saturated heterocyclyl which may contain up to 3 O, N or S, and two may fuse

together to give an optionally unsaturated or aromatic carbocyclyl or heterocyclyl containing up to 3 O, N or S, and the ring may be substituted, or an optionally substituted and optionally unsaturated or aromatic ring may be condensed with the ring; or  
 RL9+RY1, RL9+RY1asterisk = optionally unsaturated 3-7-heterocyclyl optionally containing up to 3 O, S or N;  
 WL = optionally substituted 4-11-membered mono- or polycyclic aliphatic or aromatic hydrocarbonyl, having up to 6 double bonds and up to 6 N, O, S;  
 VL, XL = CO, CONRL10, NRL10CO, SO, SO2, SO2NRL10, NRL10SO2, CS, CSNRL10, NRL10CS, CSO, OCS, COO, OCO, O, ethynylene, CHRL11OCHRL12, C(=CRL11RL12), CRL11=CRL12, CRL11(ORL13)-CHRL12, CHRL11-CRL12(ORL13), CH(NRL14SO2RL15), -CH(NRL14CORL15), CH(NRL14COORL16), CH(NRL14CONRL14'CRL15), CH(CORL15), CH(COORL16) or CH(CONRL14RL15);  
 RL10 = H, optionally substituted 1-6C-alkyl, 1-6C-alkoxyalkyl, 2-6C alkenyl, 3-12C alkynyl, CO-1-6C alkynyl, COO 1-6-alkyl or SO2-1-6C alkyl or optionally substituted 3-7C cycloalkyl, COO-alkylene-aryl, CO-alkylene-aryl, arylalkyl, CO-aryl, SO2-aryl, hetaryl, CO-hetaryl, hetarylalkyl or SO2-alkylene-aryl; or  
 RL10 and RL1, RL 2, RL 3, RL 4, RL5, RL6, RL7 or RL8 together form an optionally substituted 4-8 membered heterocyclyl, containing up to 5 O, N or S;  
 RL11, RL12 = H, OH, 1-6C alkyl, 1-4C alkoxy, 2-6C alkenyl, 2-6C alkynyl or alkylene-cycloalkyl or optionally substituted 3-7C cycloalkyl, aryl, arylalkyl, hetaryl or hetarylalkyl;  
 RL13 = H, optionally substituted 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl or alkylene-cycloalkyl or optionally substituted 3-7C-cycloalkyl, aryl, arylalkyl, hetaryl or hetarylalkyl;  
 RL14, RL14' = H, optionally substituted 1-6C alkyl, 1-6C alkoxyalkyl, 2-6C alkenyl, 3-12C alkynyl, CO-1-6C alkyl, CO-O-1-6C-alkyl-, 1-6C-alkylene-3-7C-cycloalkyl or SO2-1-6C-alkyl or optionally substituted 3-7C cycloalkyl, COO-alkylene-aryl, CO-alkylene-aryl, aryl, CO-aryl, SO2-aryl, hetaryl, CO-hetaryl, hetarylalkyl, arylalkyl or SO2-alkylene-aryl;  
 RL15 = optionally substituted 1-6C-alkyl, alkoxyalkyl, 1-6C-alkylene-3-7C-cycloalkyl, 6-12C-bicycloalkyl, 1-6C-alkylene-6-12C-bicycloalkyl, 7-20C tricycloalkyl or 1-6C alkylene-7-20C tricycloalkyl, up to 3 substituted 3-7C cycloalkyl, aryl, arylalkyl, hetarylalkyl or 3-8-membered optionally saturated or aromatic heterocyclyl which may contain up to 3 O, N or S, and where 2 groups together may form a condensed optionally saturated or aromatic carbocyclic or heterocycle, which may contain up to 3 O, N or S, and where the may be substituted or a further optionally substituted or optionally saturated or aromatic ring may be condensed on the ring; or  
 RL15+RL14, RL15+RL14asterisk = an optionally saturated 3-7C heterocyclyl, optionally containing up to 2 O, S or N;  
 RL16 = optionally substituted 1-6C-alkyl, alkoxyalkyl or 1-6C-alkylene-3-7C cycloalkyl or optionally substituted 3-7C cycloalkyl, aryl, arylalkyl, hetaryl or hetarylalkyl,  
 G = a group of formula (a);  
 the incorporation of G can be any of the 2 orientations;  
 ZG = O, S or NRG3;  
 RG1, RG2 = H, CN, NO2, halo, optionally substituted 1-6C alkyl, 2-6C alkenyl or 2-6C alkynyl, optionally substituted 1-4C alkylene-ORG4, 1-4C-alkylene-CO-ORG4, 1-4C-alkylene-CO-RG4, 1-4C-alkylene-SO2-NRG5RG6, 1-4C -alkylene-CO-NRG5RG6, 1-4C-alkylene-NRG5RG6 or 1-4C-alkylene-SRG4, optionally substituted 3-7C-cycloalkyl, 1-4C-alkylene-3-7C cycloalkyl, 1-4C alkylene-3-7C-heterocycloalkyl or 1-4C-alkylene-3-7C heterocycloalkenyl, optionally substituted aryl, arylalkyl, hetaryl or hetarylalkyl, SRG4, ORG4, SORG4, SO2-RG4, COORG4, OCORG4, O-CO-NRG5RG6, SO2NRG5RG6, CONRG5RG6, NRG5RG6 or CORG4; or  
 RG1+RG2 = optionally substituted optionally saturated or aromatic 3-9-membered carbocyclyl, carbopolycyclyl, heterocyclyl or heteropolycyclyl, containing up to 4 O, N or S;

RG3 = H, OH, CN, optionally substituted 1-6C alkyl or 1-4C-alkoxy or optionally substituted 3-7C-cycloalkyl, O-3-7C-cycloalkyl, aryl, -O-aryl, arylalkyl-or O-alkylene-aryl;

RG4 = H, optionally substituted 1-8C alkyl, 2-6C alkenyl, 2-6C alkynyl, 1-5C alkylene-1-4C alkoxy, mono or bis alkylaminoalkyl or acylaminoalkylene or optionally substituted aryl, heterocycloalkyl, heterocycloalkenyl, heteroaryl, 3-7C cycloalkyl, 1-4C alkylene heterocycloalkyl, 1-4C alkylene heterocycloalkenyl or hetarylalkyl; RG5, RG6 = H, optionally substituted 1-8C alkyl, 2-6C alkenyl, 2-6C alkynyl, 1-5C alkylene-1-4C alkoxy, mono or bis alkylaminoalkylene or acylaminoalkyl or optionally substituted aryl, heterocycloalkyl, heterocycloalkenyl, heteroaryl, 3-7C cycloalkyl, 1-4C alkylene-3-7C cycloalkyl, arylalkyl, 1-4C alkyleneheterocycloalkyl, 1-4C alkylene heterocycloalkenyl or hetarylalkyl, or SO2RG4, COORG4, CONRG4RG4asterisk or CORG4;

RG4asterisk = as for RG4;

B = a structural element containing at least one atom which can act as a hydrogen acceptor under physiological conditions, where at least one hydrogen acceptor atom along the shortest possible path on the structural element frame is at a distance of 4-13 atomic bonds to the structural element G.

Preferred Definitions:

B = A-E;

A = a structural element selected from (i) 4-8 membered monocyclic optionally saturated or aromatic hydrocarbon containing up to 4 O, N or S, where ring N or C atoms are optionally substituted and provided that at least one O, N or S is contained in A; (ii) ZA2C(=ZA1); or (iii)

NRA19RA18; or e.g. a group of formula (b);

q = 1-3;

RA18, R19 = H, optionally substituted 1-8C alkyl, 2-6C alkenyl, 2-6C alkenyl, 1-5C alkylene-1-4C alkoxy, mono or bis alkylaminoalkylene or acylaminoalkyl, or optionally substituted aryl, heterocycloalkyl, heterocycloalkenyl, hetaryl, 3-7C cycloalkyl, 1-4C alkylene-3-7C cycloalkyl, arylalkyl, 1-4C alkylene-heterocycloalkyl, 1-4C alkylene heterocycloalkenyl or hetarylalkyl or SO2RG4, COORG4, CONRG4RG4asterisk or CORG4;

E = spacer structural-element which binds A covalently with G, where the number of atomic bonds along the shortest possible path along E is 3-12;

ZA1 = O, S or optionally substituted N;

ZA2 = N, O or S.

Preferably, E = structural element of formula -(NRE1)i-E1-(UE)h-.

i, h = 0 or 1;

UE = O, S or NRE2;

RE1, RE2 = e.g. H, optionally substituted 1-6C alkyl, 1-6C alkoxyalkyl, 2-6C alkenyl, CONH-1-6C alkyl;

E1 = e.g. H, halo, OH 1-6C alkyl or 2-6C alkenyl

=> d his

(FILE 'HCAPLUS' ENTERED AT 08:30:51 ON 14 FEB 2005)

DEL HIS

FILE 'HCAPLUS' ENTERED AT 08:32:30 ON 14 FEB 2005

L1	1 S SD186 OR SD 186
L2	0 S L7418415 OR L() (7418415 OR 741 8415 OR 7418 415 OR 7 418 415)
L3	0 S SD183 OR SD 183
L4	1 S SD983 OR SD 983
L5	5 S XT199 OR XT 199
L6	2 S SG545 OR SG 545
L7	5 S SM256 OR SM 256
L8	0 S SD836 OR SD 836
L9	3 S SD7784 OR SD 7784

L10 0 S SD7783 OR SD 7783  
L11 36 S S137 OR S 137  
L12 2 S S787 OR S 787  
L13 3 S S448 OR S 448  
L14 2 S SC68448 OR SC() (68448 OR 68 448)  
L15 3 S SC56631 OR SC() (56631 OR 56 631)  
L16 2 S SC69000 OR SC() (69000 OR 69 000)  
L17 4 S SC65811 OR SC() (65811 OR 65 811)  
L18 5 S SB223245 OR SB() (223245 OR 223 245)  
L19 9 S SB265123 OR SB() (265123 OR 265 123)  
L20 0 S SB267268 OR SB() (267268 OR 267 268)  
L21 4 S SB273005 OR SB() (273005 OR 273 005)  
L22 0 S CP4632 OR CP 4632  
L23 1 S SH306 OR SH 306  
L24 4 S SB273005 OR SB() (273005 OR 273 005)  
L25 0 S SC72115 OR SC() (72115 OR 72 115)

FILE 'REGISTRY' ENTERED AT 11:07:03 ON 14 FEB 2005

L26 13 S 243972-21-6 OR 211308-14-4 OR 243672-10-8 OR 243970-98-1 OR 2  
L27 2 S 181819-14-7 OR 249298-39-3  
E C22H27N5O6S/MF  
L28 1 S E3 AND 46.150.18/RID AND NCNC3/ES AND 3/NR  
E C24H29N5O6S/MF  
L29 3 S E3 AND 46.150.18/RID AND NC5/ES AND NOC3-C6/ES AND 4/NR  
E C19H21N5O4/MF  
L30 52 S E3 AND 46.150.18/RID AND 2/NR  
L31 19 S L30 AND AMINOIMINO METHYL  
L32 8 S L31 AND BETA  
L33 3 S L32 NOT NC5/ES  
L34 1 S 188803-61-4  
E S448/CN  
E S 448/CN  
E S-448/CN  
E SB 267268/CN  
E SB-267268/CN  
E C22H24F3N3O4/MF  
L35 5 S E3 AND NC5/ES AND C6-NC6/ES AND 3/NR  
SEL RN 3 4  
L36 2 S E1-E2  
E CP 4632/CN  
E CP-4632/CN  
E C25H31FN6O5S/MF  
L37 9 S E3 AND 4/NR AND 46.150.18/RID AND NC5/ES AND NCNC3/ES  
L38 4 S L37 AND 3 FLUORO  
SEL RN 1 4  
L39 2 S E1-E2  
E SC 72115/CN  
E SC-72115/CN  
E C21H21BRCLN5O5/MF  
L40 4 S E3  
L41 2 S L40 NOT NITRO  
E C19H27N5O6/MF  
L42 34 S E3 AND 46.150.18/RID AND 1/NR  
L43 3 S L42 AND AMINO IMINO METHYL AMINO  
L44 2 S L43 AND VALINE  
L45 1 S 141028-95-7  
E C22H27N5O3/MF  
L46 2 S E3 AND 46.150.18/RID AND C6-NC2NC3/ES  
L47 1 S L46 NOT METHOXY  
E C25H33N5O6S/MF  
L48 6 S E3 AND 46.150.18/RID AND NC5/ES AND NOC3/ES AND 3/NR  
L49 2 S L48 NOT TRIMETHYL  
E C23H31N7O7/MF

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      E C22H31N7O7/MF
L51      1 S NCNC2/ES AND NC2NC2/ES AND 46.150.18/RID AND 3/NR AND 7/N AND
L52      1573 S NCNC2/ES AND NC2NC2/ES AND 46.150.18/RID AND 3/NR
L53      1236 S L52 AND 1/NC
L54      0 S L53 AND BENZOYLOXY
L55      100 S L53 AND 4 5 DIHYDRO 1H IMIDAZOL
L56      82 S L55 AND PIPERAZIN?
L57      42 S L56 NOT CL/ELS
L58      16 S L57 AND O/ELS NOT S/ELS
L59      3 S L58 AND 23-25/C
      E C25H30CLN5O5S/MF
L60      2 S E3 AND (NCNC3 AND NC5 AND C6)/ES AND 4/NR
L61      2535 S (NCNC3 AND NC5 AND C6)/ES AND 4/NR AND 1/CL AND 1/S
L62      0 S L61 AND TETRAHYDROPYRIMIDIN?
L63      2531 S L61 AND 46.150.18/RID
L64      30 S L63 AND 3 CHLORO 4
L65      4 S L64 AND TETRAHYDRO?
      SEL RN 3 4
L66      2 S E1-E2
L67      51 S L63 AND TETRAHYDRO? NOT L65
L68      24 S L67 AND 3 CHLORO
      E C22H24F3N3O4/MF
L69      5 S E3 AND NC5/ES AND C6-NC6/ES
      SEL RN 1 2
L70      2 S E1-E2
L71      36 S L26-L29,L34,L36,L39,L41,L45,L47,L49,L59,L66,L70
      E LM 609/CN
L72      1 S E3 OR VITAXIN/CN
      E ABCIXIMAB/CN
L73      1 S E3
      E XJ 735/CN
L74      1 S E3
      E XK 002/CN
L75      1 S E3
      E DMP 728/CN
L76      1 S E3
      E SK&F 107260/CN
      E SK AND F 107260/CN
      E SK/CN
      E 107260
L77      15 S E3
L78      1 S L77 AND 4/SQL
      E EMD 121974/CN
L79      1 S E3

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FILE 'HCAPIUS' ENTERED AT 11:59:56 ON 14 FEB 2005

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L80      19 S CYCLO RGDFV
L81      0 S AS PEN RGDC OH
L82      0 S AS PEN RGDC
L83      0 S PEN RGDC
L84      0 S RGDC OH
L85      61 S ?RGDC?
L86      36 S L85 NOT ?CRGDC?
L87      0 S L86 AND ASPEN?
L88      1 S L86 AND ACPEN?
L89      1 S L85 AND ACPEN?
L90      0 S L85 AND AC PEN?
L91      0 S CYCLO RGD MAMB P
L92      0 S RGD MAMB
L93      1 S RGD(L) MAMB
L94      2 S L88,L89,L93
      SEL RN

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FILE 'REGISTRY' ENTERED AT 12:07:38 ON 14 FEB 2005

L95 20 S E1-E20  
 L96 13 S L95 AND CYCLO  
 L97 12 S L96 NOT L72-L76,L78,L79  
 L98 7 S L72-L76,L78,L79  
 L99 43 S L71,L98  
 SAV L99 HADDADCOMP2/A

FILE 'HCAPLUS' ENTERED AT 12:11:35 ON 14 FEB 2005

L100 826 S L99  
 L101 1027 S LM609 OR LM 609 OR VITAXIN OR ABCIXIMAB OR C7E3 OR C7E 3 OR C  
 L102 1220 S L100,L101,L1-L25  
 ACT HADCOMP1CA/A

-----  
 L103( 10)SEA FILE=REGISTRY ABB=ON PLU=ON 208765-45-1 OR 261619-47-0 OR  
 L104( 1)SEA FILE=REGISTRY ABB=ON PLU=ON 36357-77-4  
 L105( 10)SEA FILE=REGISTRY ABB=ON PLU=ON 142375-60-8 OR 136286-50-5 OR  
 L106( 1)SEA FILE=REGISTRY ABB=ON PLU=ON 261619-50-5  
 L107( 18)SEA FILE=REGISTRY ABB=ON PLU=ON 184036-34-8 OR 215501-47-6 OR  
 L108( 5)SEA FILE=REGISTRY ABB=ON PLU=ON 154473-03-7 OR 445475-88-7 OR  
 L109( 1)SEA FILE=REGISTRY ABB=ON PLU=ON "TBC 11251"/CN  
 L110( 1)SEA FILE=REGISTRY ABB=ON PLU=ON "AC 610612"/CN  
 L111( 45)SEA FILE=REGISTRY ABB=ON PLU=ON (L103 OR L104 OR L105 OR L106  
 L112( 42)SEA FILE=REGISTRY ABB=ON PLU=ON (136286-50-5/CRN OR 136553-74  
 L113( 41)SEA FILE=REGISTRY ABB=ON PLU=ON L112 NOT MXS/CI  
 L114( 31)SEA FILE=REGISTRY ABB=ON PLU=ON L113 NOT (COMPD OR WITH)  
 L115( 76)SEA FILE=REGISTRY ABB=ON PLU=ON (L111 OR L114)  
 L116 STR  
 L117( 319)SEA FILE=REGISTRY SSS FUL L116  
 L118 STR  
 L119( 4)SEA FILE=REGISTRY SUB=L117 CSS FUL L118  
 L120( 5)SEA FILE=REGISTRY ABB=ON PLU=ON C27H25NO6/MF AND 46.150.18/RI  
 L121( 1)SEA FILE=REGISTRY ABB=ON PLU=ON L120 AND DIMETHYLAMINO  
 L122( 9)SEA FILE=REGISTRY ABB=ON PLU=ON C25H21NO6/MF AND 46.150.18/RI  
 L123( 2)SEA FILE=REGISTRY ABB=ON PLU=ON L122 AND METHOXY AND AMINOPHE  
 L124( 1)SEA FILE=REGISTRY ABB=ON PLU=ON L123 AND 3 AMINO  
 L125( 139)SEA FILE=REGISTRY ABB=ON PLU=ON N4C/ES AND NC5/ES AND NCNC3/E  
 L126( 27)SEA FILE=REGISTRY ABB=ON PLU=ON L125 AND 9/N AND S/ELS  
 L127( 7)SEA FILE=REGISTRY ABB=ON PLU=ON L126 AND 6/O  
 L128( 3)SEA FILE=REGISTRY ABB=ON PLU=ON L127 AND 27/C  
 L129( 5)SEA FILE=REGISTRY ABB=ON PLU=ON (L128 OR L121 OR L124 OR L128  
 L130( 85)SEA FILE=REGISTRY ABB=ON PLU=ON (L115 OR L119 OR L129)  
 L131 STR  
 L132( 319)SEA FILE=REGISTRY SSS FUL L131  
 L133( 65)SEA FILE=REGISTRY ABB=ON PLU=ON L132 AND 4 6 DIMETHOXY  
 L134( 31)SEA FILE=REGISTRY ABB=ON PLU=ON L133 AND 2/N AND 6/O  
 L135( 4)SEA FILE=REGISTRY ABB=ON PLU=ON L134 AND C22H22N2O6  
 L136( 68)SEA FILE=REGISTRY ABB=ON PLU=ON L132 AND 2/N AND 6/O  
 L137( 31)SEA FILE=REGISTRY ABB=ON PLU=ON L136 AND ETHOXY  
 L138( 29)SEA FILE=REGISTRY ABB=ON PLU=ON L137 AND METHOXY  
 L139( 6)SEA FILE=REGISTRY ABB=ON PLU=ON L138 AND 4 6 DIMETHYL  
 L140( 5)SEA FILE=REGISTRY ABB=ON PLU=ON L139 NOT 204267-90-3  
 L141( 64)SEA FILE=REGISTRY ABB=ON PLU=ON L132 AND 2/N AND 4/O  
 L142( 34)SEA FILE=REGISTRY ABB=ON PLU=ON L141 AND 4 6 DIMETHYL  
 L143( 9)SEA FILE=REGISTRY ABB=ON PLU=ON L142 AND METHOXY  
 L144( 2)SEA FILE=REGISTRY ABB=ON PLU=ON L143 AND C22H22N2O4  
 L145( 8)SEA FILE=REGISTRY ABB=ON PLU=ON L132 AND 2/N AND 3/O  
 L146( 2)SEA FILE=REGISTRY ABB=ON PLU=ON L145 AND C22H22N2O3  
 L147( 13)SEA FILE=REGISTRY ABB=ON PLU=ON (L135 OR L140 OR L144 OR L146  
 L148( 96)SEA FILE=REGISTRY ABB=ON PLU=ON L130 OR L147  
 L149( 1627)SEA FILE=HCAPLUS ABB=ON PLU=ON L148  
 L150( 6)SEA FILE=HCAPLUS ABB=ON PLU=ON CGS31447 OR CGS(W) (31447 OR 31  
 L151( 3)SEA FILE=HCAPLUS ABB=ON PLU=ON CGS34043 OR CGS(W) (34043 OR 34



L152 (	12) SEA FILE=HCAPLUS ABB=ON PLU=ON CGS35066 OR CGS (W) (35066 OR 35
L153 (	1) SEA FILE=HCAPLUS ABB=ON PLU=ON CGS35339 OR CGS (W) (35339 OR 35
L154 (	12) SEA FILE=HCAPLUS ABB=ON PLU=ON CGS35066 OR CGS (W) (35066 OR 35
L155 (	2) SEA FILE=HCAPLUS ABB=ON PLU=ON WS79089A OR WS (W) (79089A OR 79
L156 (	3) SEA FILE=HCAPLUS ABB=ON PLU=ON WS75624A OR WS (W) (75624A OR 75
L157 (	3) SEA FILE=HCAPLUS ABB=ON PLU=ON PD069185 OR PD (W) (069185 OR 06
L158 (	3) SEA FILE=HCAPLUS ABB=ON PLU=ON SCH54470 OR SCH (W) (54470 OR 54
L159 (	0) SEA FILE=HCAPLUS ABB=ON PLU=ON RU69296 OR RU (W) (69296 OR 69 2
L160 (	0) SEA FILE=HCAPLUS ABB=ON PLU=ON RU69739 OR RU (W) (69739 OR 69 7
L161 (	0) SEA FILE=HCAPLUS ABB=ON PLU=ON KC12792 (W) (2AB OR 2 AB) OR KC (
L162 (	5) SEA FILE=HCAPLUS ABB=ON PLU=ON SLV306 OR SLV 306
L163 (	17) SEA FILE=HCAPLUS ABB=ON PLU=ON FR901533 OR FR (W) (901533 OR 90
L164 (	0) SEA FILE=HCAPLUS ABB=ON PLU=ON POHOSPHORAMIDON?
L165 (	1373) SEA FILE=HCAPLUS ABB=ON PLU=ON PHOSPHORAMIDON?
L166 (	0) SEA FILE=HCAPLUS ABB=ON PLU=ON BROMOBENZY? (L) SULF? (L) AMINO (L)
L167 (	0) SEA FILE=HCAPLUS ABB=ON PLU=ON BROMOBENZY? (L) SULF? (L) AMINO (L)
L168 (	273) SEA FILE=HCAPLUS ABB=ON PLU=ON FR139317 OR FR (W) (139317 OR 13
L169 (	1) SEA FILE=HCAPLUS ABB=ON PLU=ON FR901367 OR FR (W) (901367 OR 90
L170 (	1) SEA FILE=HCAPLUS ABB=ON PLU=ON BE182578 OR BE (W) (182578 OR 18
L171 (	1454) SEA FILE=HCAPLUS ABB=ON PLU=ON BQ123 OR BQ 123
L172 (	111) SEA FILE=HCAPLUS ABB=ON PLU=ON TAK044 OR TAK 044
L173 (	85) SEA FILE=HCAPLUS ABB=ON PLU=ON PD142893 OR PD (W) (142893 OR 14
L174 (	8) SEA FILE=HCAPLUS ABB=ON PLU=ON PD156252 OR PD (W) (156252 OR 15
L175 (	72) SEA FILE=HCAPLUS ABB=ON PLU=ON BQ485 OR BQ 485
L176 (	4) SEA FILE=HCAPLUS ABB=ON PLU=ON COCHINMICIN# (W) (1 OR I)
L177 (	0) SEA FILE=HCAPLUS ABB=ON PLU=ON MYRICERON? (L) CAFFEIC ACID ES
L178 (	0) SEA FILE=HCAPLUS ABB=ON PLU=ON MYRICERON? (L) CAFFEIC ACID
L179 (	16) SEA FILE=HCAPLUS ABB=ON PLU=ON MYRICERON?
L180 (	4) SEA FILE=HCAPLUS ABB=ON PLU=ON MYRICERON? (L) CAFFEOYL? (L) E
L181 (	5) SEA FILE=HCAPLUS ABB=ON PLU=ON CYCLO (L) TRP (L) GLU (L) ALA (L) ALLO
L182 (	17) SEA FILE=HCAPLUS ABB=ON PLU=ON BE18257B OR BE (W) (18257B OR 18
L183 (	3) SEA FILE=HCAPLUS ABB=ON PLU=ON L181 AND L182
L184 (	22) SEA FILE=HCAPLUS ABB=ON PLU=ON BE18257# OR BE (W) (18257# OR 18
L185 (	3) SEA FILE=HCAPLUS ABB=ON PLU=ON L181 AND L184
L186 (	17) SEA FILE=HCAPLUS ABB=ON PLU=ON (L182 OR L183)
L187 (	31) SEA FILE=HCAPLUS ABB=ON PLU=ON SITAXSENTAN#
L188 (	5) SEA FILE=HCAPLUS ABB=ON PLU=ON TBC3214 OR TBC 3214
L189 (	8) SEA FILE=HCAPLUS ABB=ON PLU=ON TBC3711 OR TBC 3711
L190 (	173) SEA FILE=HCAPLUS ABB=ON PLU=ON SB209670 OR SB (W) (209670 OR 20
L191 (	654) SEA FILE=HCAPLUS ABB=ON PLU=ON BOSENTAN#
L192 (	71) SEA FILE=HCAPLUS ABB=ON PLU=ON PD156707 OR PD (W) (156707 OR 15
L193 (	15) SEA FILE=HCAPLUS ABB=ON PLU=ON "L749329" OR L (W) (749329 OR 74
L194 (	6) SEA FILE=HCAPLUS ABB=ON PLU=ON "L754142" OR L (W) (754 142 OR 7
L195 (	7) SEA FILE=HCAPLUS ABB=ON PLU=ON ENRASSENTAN#
L196 (	1) SEA FILE=HCAPLUS ABB=ON PLU=ON A127772 OR A (W) (127772 OR 127
L197 (	104) SEA FILE=HCAPLUS ABB=ON PLU=ON ABTRASSENTAN# OR ABT627 OR ABT
L198 (	3) SEA FILE=HCAPLUS ABB=ON PLU=ON EMD94246 OR EMD (W) (94246 OR 94
L199 (	9) SEA FILE=HCAPLUS ABB=ON PLU=ON ZD1611 OR ZD 1611
L200 (	3) SEA FILE=HCAPLUS ABB=ON PLU=ON K8794 OR K 8794
L201 (	24) SEA FILE=HCAPLUS ABB=ON PLU=ON A182086 OR A (W) (182086 OR 182
L202 (	1) SEA FILE=HCAPLUS ABB=ON PLU=ON PD163070 OR PD (W) (163070 OR 16
L203 (	0) SEA FILE=HCAPLUS ABB=ON PLU=ON BENZODIOXOL? (L) DIMETHYLAMINO (L
L204 (	0) SEA FILE=HCAPLUS ABB=ON PLU=ON BENZODIOXOL? (L) METHOXYPHENYL? (
L205 (	0) SEA FILE=HCAPLUS ABB=ON PLU=ON BENZODIOXOL? (L) BUTENOIC
L206 (	0) SEA FILE=HCAPLUS ABB=ON PLU=ON PD166557 OR PD (W) (166557 OR 16
L207 (	16) SEA FILE=HCAPLUS ABB=ON PLU=ON RO 61 1790
L208 (	25) SEA FILE=HCAPLUS ABB=ON PLU=ON BMS193884 OR BMS (W) (193884 OR
L209 (	9) SEA FILE=HCAPLUS ABB=ON PLU=ON BMS207940 OR BMS (W) (207940 OR
L210 (	2) SEA FILE=HCAPLUS ABB=ON PLU=ON SB209598 OR SB (W) (209598 OR 20
L211 (	1) SEA FILE=HCAPLUS ABB=ON PLU=ON SB209834 OR SB (W) (209834 OR 20
L212 (	2) SEA FILE=HCAPLUS ABB=ON PLU=ON A206377 OR A (W) (206377 OR 206
L213 (	5) SEA FILE=HCAPLUS ABB=ON PLU=ON EMD122801 OR EMD (W) (122801 OR
L214 (	60) SEA FILE=HCAPLUS ABB=ON PLU=ON TEZOSENTAN#

L215 ( 0)SEA FILE=HCAPLUS ABB=ON PLU=ON AC 61 0612  
 L216 ( 2)SEA FILE=HCAPLUS ABB=ON PLU=ON 61 0612  
 L217 ( 2)SEA FILE=HCAPLUS ABB=ON PLU=ON RO 61 0612  
 L218 ( 8)SEA FILE=HCAPLUS ABB=ON PLU=ON T0201 OR T 0201  
 L219 ( 19)SEA FILE=HCAPLUS ABB=ON PLU=ON J104132 OR J(W) (104132 OR 104  
 L220 ( 0)SEA FILE=HCAPLUS ABB=ON PLU=ON TBC11252 OR TBS(W) (11252 OR 11  
 L221 ( 10)SEA FILE=REGISTRY ABB=ON PLU=ON 208765-45-1 OR 261619-47-0 OR  
 L222 ( 1)SEA FILE=REGISTRY ABB=ON PLU=ON 36357-77-4  
 L223 ( 10)SEA FILE=REGISTRY ABB=ON PLU=ON 142375-60-8 OR 136286-50-5 OR  
 L224 ( 1)SEA FILE=REGISTRY ABB=ON PLU=ON 261619-50-5  
 L225 ( 18)SEA FILE=REGISTRY ABB=ON PLU=ON 184036-34-8 OR 215501-47-6 OR  
 L226 ( 5)SEA FILE=REGISTRY ABB=ON PLU=ON 154473-03-7 OR 445475-88-7 OR  
 L227 ( 1)SEA FILE=REGISTRY ABB=ON PLU=ON "TBC 11251"/CN  
 L228 ( 1)SEA FILE=REGISTRY ABB=ON PLU=ON "AC 610612"/CN  
 L229 ( 45)SEA FILE=REGISTRY ABB=ON PLU=ON (L221 OR L222 OR L223 OR L224  
 L230 ( 42)SEA FILE=REGISTRY ABB=ON PLU=ON (136286-50-5/CRN OR 136553-74  
 L231 ( 41)SEA FILE=REGISTRY ABB=ON PLU=ON L230 NOT MXS/CI  
 L232 ( 31)SEA FILE=REGISTRY ABB=ON PLU=ON L231 NOT (COMPD OR WITH)  
 L233 ( 76)SEA FILE=REGISTRY ABB=ON PLU=ON (L229 OR L232)  
 L234 ( 1463)SEA FILE=HCAPLUS ABB=ON PLU=ON L233  
 L235 ( 4135)SEA FILE=HCAPLUS ABB=ON PLU=ON (L150 OR L151 OR L152 OR L153  
 L236 ( 4325)SEA FILE=HCAPLUS ABB=ON PLU=ON (L234 OR L235)  
 L237 STR  
 L238 ( 319)SEA FILE=REGISTRY SSS FUL L237  
 L239 STR  
 L240 ( 4)SEA FILE=REGISTRY SUB=L238 CSS FUL L239  
 L241 ( 9)SEA FILE=HCAPLUS ABB=ON PLU=ON L240  
 L242 ( 3)SEA FILE=HCAPLUS ABB=ON PLU=ON BSF302146 OR BSF(W) (302146 OR  
 L243 ( 4329)SEA FILE=HCAPLUS ABB=ON PLU=ON (L236 OR L241 OR L242)  
 L244 ( 5)SEA FILE=REGISTRY ABB=ON PLU=ON C27H25NO6/MF AND 46.150.18/RI  
 L245 ( 1)SEA FILE=REGISTRY ABB=ON PLU=ON L244 AND DIMETHYLAMINO  
 L246 ( 9)SEA FILE=REGISTRY ABB=ON PLU=ON C25H21NO6/MF AND 46.150.18/RI  
 L247 ( 2)SEA FILE=REGISTRY ABB=ON PLU=ON L246 AND METHOXY AND AMINOPHE  
 L248 ( 1)SEA FILE=REGISTRY ABB=ON PLU=ON L247 AND 3 AMINO  
 L249 ( 139)SEA FILE=REGISTRY ABB=ON PLU=ON N4C/ES AND NC5/ES AND NCNC3/E  
 L250 ( 27)SEA FILE=REGISTRY ABB=ON PLU=ON L249 AND 9/N AND S/ELS  
 L251 ( 7)SEA FILE=REGISTRY ABB=ON PLU=ON L250 AND 6/O  
 L252 ( 3)SEA FILE=REGISTRY ABB=ON PLU=ON L251 AND 27/C  
 L253 ( 5)SEA FILE=REGISTRY ABB=ON PLU=ON (L252 OR L245 OR L248 OR L252  
 L254 ( 54)SEA FILE=HCAPLUS ABB=ON PLU=ON L253  
 L255 ( 4332)SEA FILE=HCAPLUS ABB=ON PLU=ON (L254 OR L243)  
 L256 ( 4447)SEA FILE=HCAPLUS ABB=ON PLU=ON (L149 OR L255)  
 L257 ( 2)SEA FILE=HCAPLUS ABB=ON PLU=ON AC610612 OR AC(W) (610612 OR 61  
 L258 4447 SEA FILE=HCAPLUS ABB=ON PLU=ON (L256 OR L257)  
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 L259 8 S L102 AND L258  
 L260 29925 S L102 OR INTEGRIN  
 L261 18859 S L258 OR ENDOTHELIN?

FILE 'REGISTRY' ENTERED AT 12:19:19 ON 14 FEB 2005  
 ACT HADDADCOMPDI/A  
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L262 ( 10)SEA FILE=REGISTRY ABB=ON PLU=ON 208765-45-1 OR 261619-47-0 OR  
 L263 ( 1)SEA FILE=REGISTRY ABB=ON PLU=ON 36357-77-4  
 L264 ( 10)SEA FILE=REGISTRY ABB=ON PLU=ON 142375-60-8 OR 136286-50-5 OR  
 L265 ( 1)SEA FILE=REGISTRY ABB=ON PLU=ON 261619-50-5  
 L266 ( 18)SEA FILE=REGISTRY ABB=ON PLU=ON 184036-34-8 OR 215501-47-6 OR  
 L267 ( 5)SEA FILE=REGISTRY ABB=ON PLU=ON 154473-03-7 OR 445475-88-7 OR  
 L268 ( 1)SEA FILE=REGISTRY ABB=ON PLU=ON "TBC 11251"/CN  
 L269 ( 1)SEA FILE=REGISTRY ABB=ON PLU=ON "AC 610612"/CN  
 L270 ( 45)SEA FILE=REGISTRY ABB=ON PLU=ON (L262 OR L263 OR L264 OR L265  
 L271 ( 42)SEA FILE=REGISTRY ABB=ON PLU=ON (136286-50-5/CRN OR 136553-74  
 L272 ( 41)SEA FILE=REGISTRY ABB=ON PLU=ON L271 NOT MXS/CI

L273 ( 31)SEA FILE=REGISTRY ABB=ON PLU=ON L272 NOT (COMP D OR WITH)  
 L274 ( 76)SEA FILE=REGISTRY ABB=ON PLU=ON (L270 OR L273)  
 L275 STR  
 L276 ( 319)SEA FILE=REGISTRY SSS FUL L275  
 L277 STR  
 L278 ( 4)SEA FILE=REGISTRY SUB=L276 CSS FUL L277  
 L279 ( 5)SEA FILE=REGISTRY ABB=ON PLU=ON C27H25NO6/MF AND 46.150.18/RI  
 L280 ( 1)SEA FILE=REGISTRY ABB=ON PLU=ON L279 AND DIMETHYLAMINO  
 L281 ( 9)SEA FILE=REGISTRY ABB=ON PLU=ON C25H21NO6/MF AND 46.150.18/RI  
 L282 ( 2)SEA FILE=REGISTRY ABB=ON PLU=ON L281 AND METHOXY AND AMINOPHE  
 L283 ( 1)SEA FILE=REGISTRY ABB=ON PLU=ON L282 AND 3 AMINO  
 L284 ( 139)SEA FILE=REGISTRY ABB=ON PLU=ON N4C/ES AND NC5/ES AND NCNC3/E  
 L285 ( 27)SEA FILE=REGISTRY ABB=ON PLU=ON L284 AND 9/N AND S/ELS  
 L286 ( 7)SEA FILE=REGISTRY ABB=ON PLU=ON L285 AND 6/O  
 L287 ( 3)SEA FILE=REGISTRY ABB=ON PLU=ON L286 AND 27/C  
 L288 ( 5)SEA FILE=REGISTRY ABB=ON PLU=ON (L287 OR L280 OR L283 OR L287  
 L289 ( 85)SEA FILE=REGISTRY ABB=ON PLU=ON (L274 OR L278 OR L288)  
 L290 STR  
 L291 ( 319)SEA FILE=REGISTRY SSS FUL L290  
 L292 ( 65)SEA FILE=REGISTRY ABB=ON PLU=ON L291 AND 4 6 DIMETHOXY  
 L293 ( 31)SEA FILE=REGISTRY ABB=ON PLU=ON L292 AND 2/N AND 6/O  
 L294 ( 4)SEA FILE=REGISTRY ABB=ON PLU=ON L293 AND C22H22N2O6  
 L295 ( 68)SEA FILE=REGISTRY ABB=ON PLU=ON L291 AND 2/N AND 6/O  
 L296 ( 31)SEA FILE=REGISTRY ABB=ON PLU=ON L295 AND ETHOXY  
 L297 ( 29)SEA FILE=REGISTRY ABB=ON PLU=ON L296 AND METHOXY  
 L298 ( 6)SEA FILE=REGISTRY ABB=ON PLU=ON L297 AND 4 6 DIMETHYL  
 L299 ( 5)SEA FILE=REGISTRY ABB=ON PLU=ON L298 NOT 204267-90-3  
 L300 ( 64)SEA FILE=REGISTRY ABB=ON PLU=ON L291 AND 2/N AND 4/O  
 L301 ( 34)SEA FILE=REGISTRY ABB=ON PLU=ON L300 AND 4 6 DIMETHYL  
 L302 ( 9)SEA FILE=REGISTRY ABB=ON PLU=ON L301 AND METHOXY  
 L303 ( 2)SEA FILE=REGISTRY ABB=ON PLU=ON L302 AND C22H22N2O4  
 L304 ( 8)SEA FILE=REGISTRY ABB=ON PLU=ON L291 AND 2/N AND 3/O  
 L305 ( 2)SEA FILE=REGISTRY ABB=ON PLU=ON L304 AND C22H22N2O3  
 L306 ( 13)SEA FILE=REGISTRY ABB=ON PLU=ON (L294 OR L299 OR L303 OR L305  
 L307 96 SEA FILE=REGISTRY ABB=ON PLU=ON L289 OR L306  
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FILE 'HCAPLUS' ENTERED AT 12:19:36 ON 14 FEB 2005

L308 1627 S L307  
 L309 18859 S L261 OR L308  
 L310 196 S L260 AND L309  
 L311 83 S L310 AND (PY<=2000 OR PRY<=2000 OR AY<=2000)  
 L312 20 S L311 AND (ALPHAV OR ALPHA5 OR ALPHA() (V OR 5))  
 L313 27 S L311 AND (BETA3 OR BETAI III OR BETA() (3 OR III))  
 L314 14 S L312 AND L313

FILE 'REGISTRY' ENTERED AT 12:21:34 ON 14 FEB 2005

L315 1 S 116243-73-3

FILE 'HCAPLUS' ENTERED AT 12:21:50 ON 14 FEB 2005

L316 18859 S L315 OR L261 OR L309  
 L317 14 S L316 AND L314  
 L318 14 S L317 AND ENDOTHELIN  
 SEL DN AN 5 12  
 L319 2 S L318 AND E21-E26

FILE 'HCAPLUS' ENTERED AT 12:24:12 ON 14 FEB 2005

SEL PN 1

FILE 'WPIX' ENTERED AT 12:25:11 ON 14 FEB 2005

L320 2 S E27-E25  
 L321 1 S L320 NOT EYEWEAR  
 L322 3047 S A61K045-06/IPC

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L323      15 S L322 AND (ALPHAV OR ALPHA5 OR ALPHA() (V OR 5) ) (L) (BETA3 OR BE
L324      33 S L322 AND ENDOTHELIN?/BIX
L325      2 S L323 AND L324
L326      10 S L322 AND (ALPHAVBETA3 OR ALPHA5BETA3 OR ALPHA5BETAI III OR ALPH
L327      2 S L324 AND L326
L328      3 S L325,L327
L329      36 S L322 AND INTEGRIN?/BIX
L330      6 S L329 AND L324
L331      6 S L328,L330
L332      1 S L331 AND PY<=2000
L333      4 S L331 AND PRY<=2000
L334      4 S L331 AND AY<=2000
L335      4 S L332-L334,L321
          SEL DN AN 1 2
L336      2 S L335 NOT E36-E39
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FILE 'WPIX' ENTERED AT 12:41:53 ON 14 FEB 2005

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